To. Jan

BEST AVAILABLE COPY

Access DB# 92990

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Brian Kwon Examiner #: 78155 Date: 5/1/03
Art Unit: 1614 Phone Number 30 8-5311 Serial Number: 10/056,286
Mail Box and Bldg/Room Location: 3D04 Results Format Preferred (circle): PAPER DISK E-MAIL
CM1

If more than one search is submitted, please prioritize searches in order of need. mej

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: use of inhibitors of soluble Epoxide hydrolase etc..

Inventors (please provide full names): Wein et al

Earliest Priority Filing Date: 1/02

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

see attached

- a method inhibiting the proliferation of VSM.
  - i) derivative of urea (e.g. CDU, DCU) claim 5
  - ii) lipid alkoxide (claim 7)
  - iii) dicyclohexylcarbodiide (claim 8)
  - iv) phenyl glycidol (e.g. 5,5-4 nitrophenylglycidol) claim 9.
  - v) chalcone oxide (e.g. 4-phenylchalcone oxide, 4-fluorochalcone oxide).

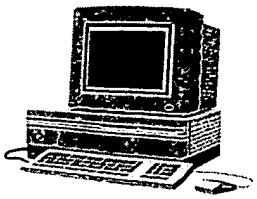
further comprising cis-Epoxyeicosatrienoic acid (claim 17)

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Jan	NA Sequence (#)	STN ✓
Searcher Phone #: 4454	AA Sequence (#)	Dialog
Searcher Location:	Structure (#) ✓	Questel/Orbit
Date Searcher Picked Up: 5/5/03	Bibliographic ✓	Dr.Link
Date Completed: 5/5/03	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time: 30	Patent Family	WWW/Internet
Online Time: + 75	Other	Other (specify)

PTO-1590 (8-01)

BioTech-Chem Library
Search Results
Feedback Form (Optional)



Scientific & Technical Information Center

The search results generated for your recent request are attached. If you have any questions or comments (compliments or complaints) about the scope or the results of the search, please contact ***the BioTech-Chem searcher*** who conducted the search ***or contact***:

Mary Hale, Supervisor, 308-4258
CM-1 Room 1E01

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* *(Example: 1610)*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

  Types of relevant prior art found:
  - ☐ Foreign Patent(s)
  - ☐ Non-Patent Literature
    (journal articles, conference proceedings, new product announcements etc.)
- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Search results were not useful in determining patentability or understanding the invention.

Other Comments:

Drop off completed forms at the **Circulation Desk CM-1,** or send to Mary Hale, **CM1-1E01 or e-mail mary.hale@uspto.gov.**

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 17:36:10 ON 05 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    4 MAY 2003  HIGHEST RN 510703-80-7
DICTIONARY FILE UPDATES:   4 MAY 2003  HIGHEST RN 510703-80-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide.can

L88  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   57-13-6  REGISTRY
CN   Urea (8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Aquacare
CN   Aquadrate
CN   B-I-K
CN   Basodexan
CN   Benural 70
CN   Carbamide
CN   Carbamimidic acid
CN   Carbonyl diamide
CN   Elaqua XX
CN   Eucerin 10% Urea Lotion
CN   Hyanit
CN   Isourea
CN   Keratinamin
CN   Keratinamin Kowa
CN   Nutraplus
CN   Onychomal
CN   Optigen 1200
CN   Pastaron
CN   Pastaron 10
CN   Pastaron 20
CN   Pastaron 20 soft
CN   Pseudourea
CN   UR
CN   Urea perhydrate
CN   Ureaphil
CN   Ureophil
CN   Urepeal
CN   Urepeal L
CN   Urepearl
CN   Urevert
CN   Varioform II
FS   3D CONCORD
DR   30535-50-3
```
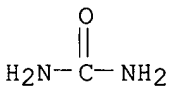

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

MF C H4 N2 O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

60370 REFERENCES IN FILE CA (1957 TO DATE)
3020 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
60404 REFERENCES IN FILE CAPLUS (1957 TO DATE)
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:296786

REFERENCE 2: 138:296597

REFERENCE 3: 138:296368

REFERENCE 4: 138:294819

REFERENCE 5: 138:294582

REFERENCE 6: 138:293383

REFERENCE 7: 138:293022

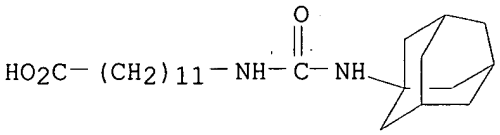
REFERENCE 8: 138:292840

REFERENCE 9: 138:292784

REFERENCE 10: 138:292745

=> d l61 ide can

L61 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2003 ACS
RN 479413-70-2 REGISTRY
CN Dodecanoic acid, 12-[[(tricyclo[3.3.1.13,7]dec-1-ylamino)carbonyl]amino]-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H40 N2 O3
SR CA
LC STN Files: CA, CAPLUS



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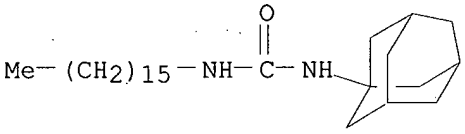
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:49365

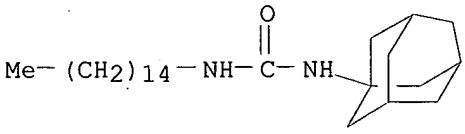
=> d l61 ide can 2-5

L61 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2003 ACS
RN 327971-66-4 REGISTRY
CN Urea, N-hexadecyl-N'-tricyclo[3.3.1.13,7]dec-1-yl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H50 N2 O
SR Chemical Library
LC STN Files: CHEMCATS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L61 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2003 ACS
RN 120615-90-9 REGISTRY
CN Urea, N-pentadecyl-N'-tricyclo[3.3.1.13,7]dec-1-yl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H48 N2 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS



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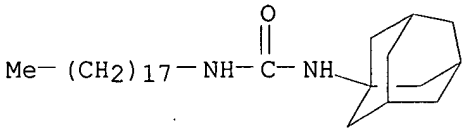
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 110:212200

L61 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2003 ACS
RN 73405-13-7 REGISTRY
CN Urea, N-octadecyl-N'-tricyclo[3.3.1.13,7]dec-1-yl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H54 N2 O
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



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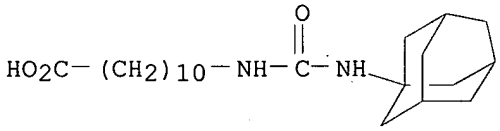
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 92:180710

L61 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2003 ACS
RN 33200-19-0 REGISTRY
CN Undecanoic acid, 1-[[(tricyclo[3.3.1.13,7]dec-1-ylamino)carbonyl]amino]-
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Undecanoic acid, 11-[3-(1-adamantyl)ureido]- (8CI)
FS 3D CONCORD
MF C22 H38 N2 O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)



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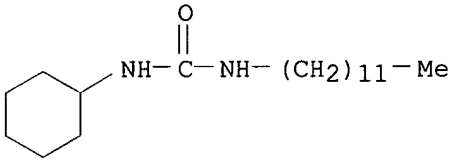
2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 78:71571

REFERENCE 2: 75:48734

=> d ide can l63

L63 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **402939-18-8** REGISTRY
CN Urea, N-cyclohexyl-N'-dodecyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C19 H38 N2 O
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1957 TO DATE)
4 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:231736

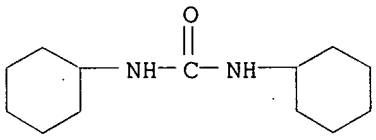
REFERENCE 2: 138:49365

REFERENCE 3: 137:88154

REFERENCE 4: 136:228661

=> d ide can l29

L29 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **2387-23-7** REGISTRY
CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Urea, 1,3-dicyclohexyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 1,3-Dicyclohexylurea
CN Dicyclohexylcarbodiamide
CN N,N'-Dicyclohexylurea
FS 3D CONCORD
MF C13 H24 N2 O
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MSDS-OHS, SPECINFO, SYNTHLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

339 REFERENCES IN FILE CA (1957 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
339 REFERENCES IN FILE CAPLUS (1957 TO DATE)
44 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:267583

REFERENCE 2: 138:231736

REFERENCE 3: 138:204645

REFERENCE 4: 138:182942

REFERENCE 5: 138:182263

REFERENCE 6: 138:173298

REFERENCE 7: 138:153330

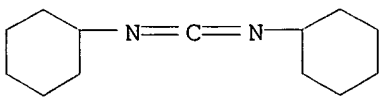
REFERENCE 8: 138:136558

REFERENCE 9: 138:49365

REFERENCE 10: 138:15240

=> d ide can l44

L44 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **538-75-0** REGISTRY
CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Carbodiimide, dicyclohexyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 1,3-Dicyclohexylcarbodiimide
CN Bis(cyclohexyl)carbodiimide
CN DCC
CN DCCD
CN DCCI
CN Dicyclohexylcarbodiimide
CN N,N'-Dicyclohexylcarbodiimide
CN N,N'-Methanetetraylbis[cyclohexanamine]
FS 3D CONCORD
MF C13 H22 N2
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



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3245 REFERENCES IN FILE CA (1957 TO DATE)
65 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3252 REFERENCES IN FILE CAPLUS (1957 TO DATE)
31 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:292417

REFERENCE 2: 138:290394

REFERENCE 3: 138:288241

REFERENCE 4: 138:287911

REFERENCE 5: 138:287249

REFERENCE 6: 138:271540

REFERENCE 7: 138:271246

REFERENCE 8: 138:267583

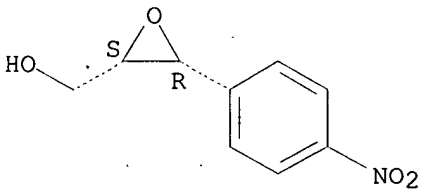
REFERENCE 9: 138:255621

REFERENCE 10: 138:255584

=> d ide can 149 tot

L49 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 143058-48-4 REGISTRY
CN **Oxiranemethanol, 3-(4-nitrophenyl)-, (2S-cis)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C9 H9 N O4**
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



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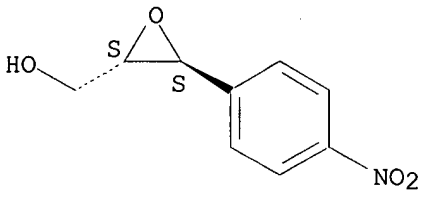
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 117:111338

L49 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 37141-34-7 REGISTRY
CN **Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)-rel- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Oxiranemethanol, 3-(4-nitrophenyl)-, trans-(.+-.)-**
OTHER NAMES:
CN **DL-trans-1-p-Nitrophenyl-1,2-epoxy-3-propanol**
CN **Oxiranemethanol, 3-(4-nitrophenyl)-, trans-**
CN **trans-1-p-Nitrophenyl-1,2-epoxy-3-propanol**

CN **trans-3-(4-Nitrophenyl)oxiranemethanol**
FS STEREOSEARCH
DR 129830-80-4
MF **C9 H9 N O4**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, USPATFULL
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1957 TO DATE)
5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:231736

REFERENCE 2: 122:329493

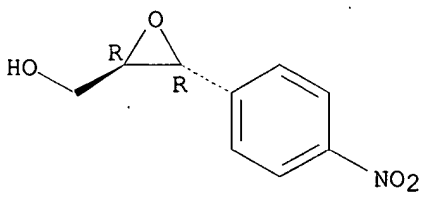
REFERENCE 3: 78:71694

REFERENCE 4: 78:71663

REFERENCE 5: 77:61532

L49 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN **37141-32-5** REGISTRY
CN **Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Oxiranemethanol, 3-(4-nitrophenyl)-, (2R-trans)-**
OTHER NAMES:
CN **(2R,3R)-(+)-3-(4-Nitrophenyl)glycidol**
CN **L-(+)-trans-1-p-Nitrophenyl-1,2-epoxy-3-propanol**
FS STEREOSEARCH
MF **C9 H9 N O4**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, MSDS-OHS, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11 REFERENCES IN FILE CA (1957 TO DATE)
11 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:231736

REFERENCE 2: 134:42084

REFERENCE 3: 129:105945

REFERENCE 4: 122:329493

REFERENCE 5: 119:43970

REFERENCE 6: 119:8612

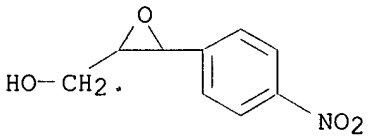
REFERENCE 7: 118:208242

REFERENCE 8: 117:2509

REFERENCE 9: 115:272840

REFERENCE 10: 78:71666

L49 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 35587-52-1 REGISTRY
CN **Oxiranemethanol, 3-(4-nitrophenyl)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **1-Propanol, 2,3-epoxy-3-(p-nitrophenyl)- (6CI, 7CI)**
OTHER NAMES:
CN **1-(p-Nitrophenyl)-1,2-epoxy-3-propanol**
FS 3D CONCORD
MF **C9 H9 N O4**
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1957 TO DATE)
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2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 120:263215

REFERENCE 2: 115:46453

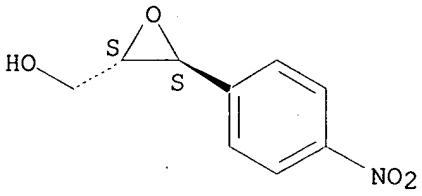
REFERENCE 3: 78:71662

REFERENCE 4: 76:126756

L49 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN **1885-07-0** REGISTRY
CN **Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN **1-Propanol, 2,3-epoxy-3-(p-nitrophenyl)-, trans-(-)- (8CI)**
CN **Oxiranemethanol, 3-(4-nitrophenyl)-, (2S-trans)-**
OTHER NAMES:
CN **(2S,3S)-(-)-3-(4-Nitrophenyl)glycidol**
CN **D-(-)-trans-1-p-Nitrophenyl-1,2-epoxy-3-propanol**
FS STEREOSEARCH
MF **C9 H9 N O4**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

14 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
14 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:231736

REFERENCE 2: 136:102181

REFERENCE 3: 134:42084

REFERENCE 4: 129:105945

REFERENCE 5: 128:201056

REFERENCE 6: 122:329493

REFERENCE 7: 119:43970

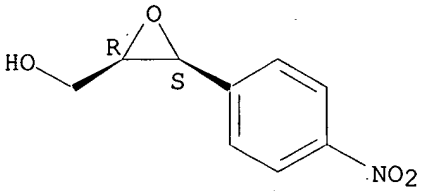
REFERENCE 8: 118:208242

REFERENCE 9: 118:81235

REFERENCE 10: 117:2509

L49 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 1885-06-9 REGISTRY
CN **Oxiranemethanol, 3-(4-nitrophenyl)-, (2R-cis)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **1-Propanol, 2,3-epoxy-3-(p-nitrophenyl)-, cis-(+)- (8CI)**
OTHER NAMES:
CN **cis-(+)-3-(4-Nitrophenyl)oxiranemethanol**
FS STEREOSEARCH
MF **C9 H9 N O4**
LC STN Files: BEILSTEIN*
(*File contains numerically searchable property data)

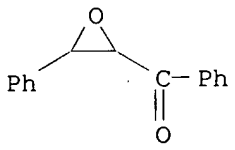
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

=> d ide can 134

L34 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **5411-12-1** REGISTRY
CN Methanone, phenyl(3-phenyloxiranyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Propiophenone, 2,3-epoxy-3-phenyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 1,3-Diphenyl-2,3-epoxy-1-propanone
CN 1-Benzoyl-2-phenyloxirane
CN 2,3-Epoxy-1,3-diphenyl-1-propanone
CN 2,3-Epoxy-3-phenylpropiophenone
CN Chalcone epoxide
CN Chalcone oxide
CN Epoxybenzalacetophenone
FS 3D CONCORD
MF C15 H12 O2
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, DETHERM*, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

154 REFERENCES IN FILE CA (1957 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
155 REFERENCES IN FILE CAPLUS (1957 TO DATE)
14 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:237786

REFERENCE 2: 137:279032

REFERENCE 3: 137:140396

REFERENCE 4: 136:38024

REFERENCE 5: 135:288644

REFERENCE 6: 134:178408

REFERENCE 7: 134:4819

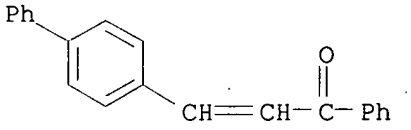
REFERENCE 8: 133:277960

REFERENCE 9: 133:207753

REFERENCE 10: 133:89527

=> d ide can l35

L35 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **2403-28-3** REGISTRY
CN 2-Propen-1-one, 3-[1,1'-biphenyl]-4-yl-1-phenyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Chalcone, 4-phenyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 4-Phenylchalcone
FS 3D CONCORD
MF C21 H16 O
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

33 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
33 REFERENCES IN FILE CAPLUS (1957 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:116492

REFERENCE 2: 135:76687

REFERENCE 3: 129:256849

REFERENCE 4: 125:43887

REFERENCE 5: 120:149635

REFERENCE 6: 116:128292

REFERENCE 7: 112:155566

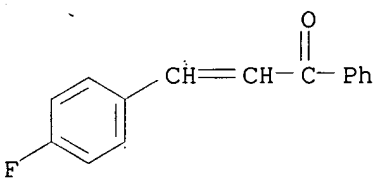
REFERENCE 8: 110:57712

REFERENCE 9: 104:201986

REFERENCE 10: 102:76014

=> d ide can l36

L36 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **1608-51-1** REGISTRY
CN 2-Propen-1-one, 3-(4-fluorophenyl)-1-phenyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Chalcone, 4-fluoro- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 4-Fluorochalcone
CN p-Fluorostyryl phenyl ketone
CN Phenyl p-fluorostyryl ketone
FS 3D CONCORD
MF C15 H11 F O
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, HODOC*, IFICDB, IFIPAT, IFIUDB, SPECINFO, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

68 REFERENCES IN FILE CA (1957 TO DATE)
68 REFERENCES IN FILE CAPLUS (1957 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:262774

REFERENCE 2: 137:228474

REFERENCE 3: 136:332664

REFERENCE 4: 135:268889

REFERENCE 5: 134:366632

REFERENCE 6: 134:193210

REFERENCE 7: 133:249544

REFERENCE 8: 133:217539

REFERENCE 9: 133:207753

REFERENCE 10: 133:89124

=> d ide can l71

L71 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **97717-69-6** REGISTRY

CN Eicosatrienoic acid, epoxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Epoxyeicosatrienoic acid
MF C20 H32 O3
CI IDS
SR CA
LC STN Files: BIOSIS, BIOTECHNO, CA, CAPLUS, EMBASE, TOXCENTER, USPAT2, USPATFULL

CM 1

CRN 97717-68-5
CMF C20 H38 O3
CCI IDS

$HO_2C-(CH_2)_{18}-Me$

D1-O-D1

95 REFERENCES IN FILE CA (1957 TO DATE)
18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
95 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:231736

REFERENCE 2: 138:199178

REFERENCE 3: 138:150826

REFERENCE 4: 138:70306

REFERENCE 5: 137:349565

REFERENCE 6: 137:198627

REFERENCE 7: 137:120467

REFERENCE 8: 137:28024

REFERENCE 9: 136:338693

REFERENCE 10: 136:272910

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 17:39:23 ON 05 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 5 May 2003 VOL 138 ISS 19
FILE LAST UPDATED: 4 May 2003 (20030504/ED)

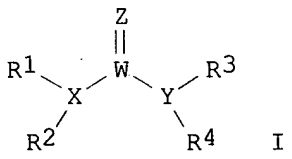
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot l90

L90 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **2003:197917** HCAPLUS
DN **138:231736**
TI Inhibitors of **epoxide hydrolases** for the treatment of hypertension
IN Kroetz, Deanna L.; Zeldin, Darryl C.; **Hammock, Bruce D.**; Morisseau, Christophe
PA Regents of the University of California, USA
SO U.S., 36 pp., Cont.-in-part of U.S. 6,150,415.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-335
NCL 514475000; 514529000; 514551000; 514625000; 514613000; 514631000; 514596000; 514588000; 514595000
CC 1-8 (Pharmacology)
Section cross-reference(s): 7, 14, 63
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6531506	B1	20030311	US 2000-721261	20001121
	US 5955496	A	19990921	US 1997-909523	19970812
	US 6150415	A	20001121	US 1999-252148	19990218
PRAI	US 1996-23397P	P	19960813		
	US 1997-909523	A2	19970812		
	US 1999-252148	A2	19990218		

OS MARPAT 138:231736
GI



I

AB The invention provides compds. that inhibit **epoxide hydrolase** in therapeutic applications for the treatment of hypertension. A preferred class of compds. for practicing the invention have the structure shown by Formula [(R1)(R2)XW(Z)Y(R3)(R4)], wherein Z is oxygen or sulfur, W is carbon phosphorous or sulfur, X and Y is each independently nitrogen, oxygen, or sulfur, and X can further be carbon, at least one of R1-R4 is hydrogen, R2 is hydrogen when X is nitrogen but is not present when X is sulfur or oxygen, R4 is hydrogen when Y is nitrogen but is not present when Y is sulfur or oxygen, R1 and R3 is each independently C1-C20 substituted or unsubstituted alkyl, cycloalkyl, aryl, acyl, or heterocyclic.
ST **epoxide hydrolase** inhibitor antihypertensive design human pregnancy hypertension
IT Pregnancy

(-induced hypertension; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT Enzyme functional sites
(active; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT Kidney
(cortex; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT Antihypertensives
Drug design
Human
Hypertension
Kidney
Microsome
Mouse
Rat
Urine
(**epoxide hydrolases** inhibitors for treatment of hypertension)

IT Fatty acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxide hydrolases** inhibitors for treatment of hypertension)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunoreactive; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT Diagnosis
(of hypertension or risk for hypertension; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT Drug delivery systems
(oral; **epoxide hydrolases** inhibitors for treatment of hypertension)

IT 60-33-3, Linoleic acid, biological studies **9048-63-9**, **Epoxide hydrolase 97717-69-6**, **Epoxyeicosatrienoic** acid 192461-94-2 192461-95-3 192461-96-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxide hydrolases** inhibitors for treatment of hypertension)

IT 101-20-2 **538-75-0** 886-59-9 1142-07-0 1145-53-5 1220-01-5 **1885-07-0** 2222-58-4 **2387-23-7** 3218-00-6 4300-43-0 7570-86-7 13074-28-7 13256-78-5 17427-95-1 17661-70-0 20258-07-5 25855-24-7 27729-98-2 29559-44-2 31510-11-9 34583-53-4 36598-10-4 **37141-32-5** **37141-34-7** 38652-23-2 53120-54-0 58490-15-6 60392-17-8 60392-18-9 62972-70-7 70243-17-3 70622-91-2 72802-45-0 72802-46-1 75461-45-9 80251-18-9 82389-34-2 82499-65-8 89609-46-1 91990-71-5 92373-98-3 98819-68-2 101452-64-6 104196-23-8 108195-84-2 109246-29-9 111681-31-3 118389-04-1 120615-85-2 124949-24-2 128276-09-5 131519-56-7 148806-83-1 148806-87-5 158072-24-3 176327-83-6 179539-07-2 195451-88-8 196791-88-5 197357-33-8 197455-83-7 200058-85-1 200059-00-3 201014-78-0 204922-97-4 246165-79-7 272449-13-5 287185-28-8 287185-29-9 303092-06-0 306746-73-6 306770-63-8 306770-65-0 306770-66-1 306770-67-2 306770-68-3 306770-69-4 306770-70-7 306770-71-8 326003-50-3 338797-32-3 338797-34-5 339170-08-0 392713-22-3 400839-30-7 401598-13-8 **402939-18-8** 446848-38-0 447429-19-8 460745-85-1 479412-88-9 479413-00-8 479413-14-4 479413-19-9 479413-39-3 479413-45-1 479413-68-8 501003-69-6 501003-70-9 501003-71-0 501003-72-1 501003-73-2 501003-74-3 501003-75-4 501003-76-5 501003-77-6 501003-78-7 501003-79-8 501003-80-1 501003-81-2 501003-82-3 501003-83-4 501003-84-5 501003-85-6 501003-86-7 501003-87-8 501003-88-9 501003-89-0 501003-90-3

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501004-01-9 501004-02-0 501004-03-1 501004-04-2 501004-05-3
501004-06-4 501004-07-5 501004-08-6 501004-09-7 501004-10-0
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501004-16-6 501004-17-7 501004-18-8 501004-19-9 501004-20-2
501011-71-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**epoxide hydrolases** inhibitors for treatment of hypertension)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(3) Black; Journal of Agricultural and Food Chemistry 1973, V21(5), P747 HCAPLUS
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(7) Cheung; Chapter 18 in The Impact of Chemistry on Biotechnology:Multidisciplinary Discussions, ASC Symposium Series No 362 1988, P217 HCAPLUS
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(22) Hitz; Abstract from the 13th International Symposium of Plant Lipids 1998
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(25) Kiyosue; The Plant Journal 1994, V6(2), P259 HCAPLUS
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(27) Lee; Science 1998, V280, P915 MEDLINE
(28) Moghaddam; Biochimica et Bio-physica Acta 1996, V1290, P327 HCAPLUS
(29) Moghaddam; Nature Medicine 1997, V3(5), P562 HCAPLUS
(30) Morisseau; Archives of Biochemistry and Biophysics 1998, V356(2), P214 HCAPLUS
(31) Mullin; Archives of Biochemistry and Biophysics 1982, V216(2), P423 HCAPLUS
(32) Mullin, C; Journal of Chemical Ecology 1988, V14(10), P1867 HCAPLUS
(33) Mumby; Agricultural and Food Chemistry 1979, V27(6), P1223 HCAPLUS
(34) Murray; Cancer 1993, V71(1), P36 MEDLINE
(35) Murray; Journal of Pathology 1995, V177, P147 HCAPLUS
(36) Pinot; Mycopathologia 1997, V140, P51 HCAPLUS
(37) Prestwich; Proc Natl Acad Sci USA 1985, V82, P1663 HCAPLUS
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(39) Stark; Phytochemistry 1995, V38(1), P31 HCAPLUS
(40) Taton; Phytochemistry 1996, V43(1), P75 HCAPLUS
(41) Theyer; The Journal of Urology 1993, V150, P1544 MEDLINE

(42) Wixtrom; Analytical Biochemistry 1988, V169, P71 HCAPLUS
(43) Wixtrom; Biochemical Pharmacology and Toxicology, vol 1: Methodological Aspects of Drug Metabolizing Enzymes 1985, P1 HCAPLUS

IT **9048-63-9, Epoxide hydrolase**
97717-69-6, Epoxyeicosatrienoic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxide hydrolases** inhibitors for treatment of hypertension)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 97717-69-6 HCAPLUS
CN Eicosatrienoic acid, epoxy- (9CI) (CA INDEX NAME)

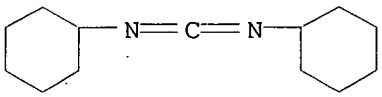
CM 1

CRN 97717-68-5
CMF C20 H38 O3
CCI IDS

$HO_2C-(CH_2)_{18}-Me$

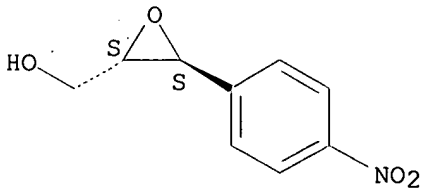
D1—O—D1

IT **538-75-0 1885-07-0 2387-23-7**
37141-32-5 37141-34-7 402939-18-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**epoxide hydrolases** inhibitors for treatment of hypertension)
RN 538-75-0 HCAPLUS
CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)

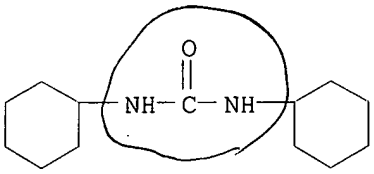


RN 1885-07-0 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

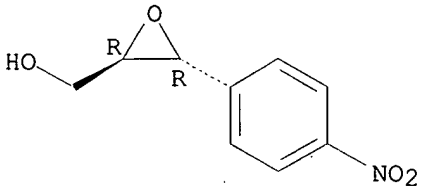


RN 2387-23-7 HCAPLUS
CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



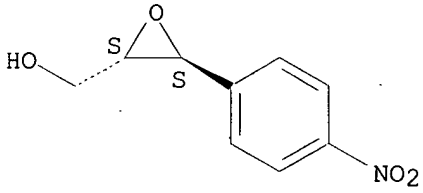
RN 37141-32-5 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

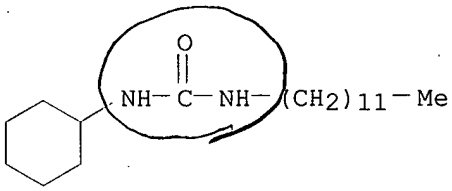


RN 37141-34-7 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 402939-18-8 HCAPLUS
CN Urea, N-cyclohexyl-N'-dodecyl- (9CI) (CA INDEX NAME)



L90 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:854210** HCAPLUS
DN **138:267583**
TI Urea and amide-based inhibitors of the juvenile hormone **epoxide hydrolase** of the tobacco hornworm (Manduca sexta: Sphingidae)
AU Severson, Tonya F.; Goodrow, Marvin H.; Morisseau, Christophe; Dowdy, Deanna L.; **Hammock, Bruce D.**
CS Department of Entomology and Cancer Research Center, University of California, Davis, CA, 95616, USA
SO Insect Biochemistry and Molecular Biology (2002), 32(12), 1741-1756
CODEN: IBMBES; ISSN: 0965-1748
PB Elsevier Science Ltd.
DT Journal
LA English
CC 7-3 (Enzymes)

Section cross-reference(s): 12

AB A new class of inhibitors of juvenile hormone **epoxide hydrolase** (JHEH) of Manduca sexta and further in vitro characterization of the enzyme are reported. The compds. are based on urea and amide pharmacophores that were previously demonstrated as effective inhibitors of mammalian sol. and microsomal **epoxide hydrolases**. The best inhibitors against JHEH activity so far within this class are N-[(Z)-9-octadecenyl]-N'-propylurea and N-hexadecyl-N'-propylurea, which inhibited hydrolysis of a surrogate substrate (t-DPPO) with an IC50 around 90 nM. The importance of substitution no. and type was investigated and results indicated that N, N'-disubstitution with asym. alkyl groups was favored. Potencies of pharmacophores decreased as follows: amide>urea>carbamate>carbodiimide>thiourea and thiocarbamate for N,N'-disubstituted compds. with sym. substituents, and urea>amide>carbamate for compds. with asym. N,N'-substituents. JHEH hydrolyzes t-DPPO with a Km of 65.6 .mu.M and a Vmax of 59 nmol min-1 mg-1 and has a substantially lower Km of 3.6 .mu.M and higher Vmax of 322 nmol min-1 mg-1 for JH III. Although none of these compds. were potent inhibitors of hydrolysis of JH III by JHEH, they are the first leads toward inhibitors of JHEH that are not potentially subject to metab. through epoxide degrdn.

ST juvenile hormone **epoxide hydrolase** inhibitor tobacco hornworm Manduca

IT Structure-activity relationship
(enzyme-inhibiting; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (Manduca sexta))

IT Juvenile hormones
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(kinetic parameters; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (Manduca sexta))

IT Optical refraction
(molar refraction, of juvenile hormones; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (Manduca sexta))

IT Enzyme kinetics
(of inhibition; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (Manduca sexta))

IT Manduca sexta
Michaelis constant
(urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (Manduca sexta))

IT **57-13-6**, Urea, biological studies 102-07-8, 1,3-Diphenylurea 111-26-2, 1-Hexanamine 111-68-2, 1-Heptanamine 112-20-9, 1-Nonanamine 112-90-3, cis-9-Octadecenylamine 124-22-1, 1-Dodecanamine 124-30-1, 1-Octadecanamine 143-27-1, 1-Hexadecanamine 301-02-0, Oleamide **538-75-0** 598-94-7, N,N-Dimethylurea 623-95-0, 1,3-Dipropylurea 632-22-4, Tetramethylurea 698-90-8, Cyclohexylurea 886-59-9, 1-Cyclohexyl-3-phenylurea 1212-29-9 2016-57-1, 1-Decanamine 2158-09-0, Dodecylurea **2387-23-7**, 1,3-**Dicyclohexylurea** 2869-34-3, 1-Tridecanamine 3359-39-5 7307-55-3, 1-Undecanamine 20258-07-5 25855-24-7 31510-11-9 55398-22-6 70243-17-3 72802-45-0 72802-46-1 118389-04-1 128276-09-5, 1-Octyl-3-propylurea 147642-79-3 158072-24-3 246165-77-5 246165-79-7 347907-04-4 348594-28-5 392713-22-3 460745-85-1 479413-19-9 500346-45-2 501003-81-2 501003-96-9 501003-98-1 503114-33-8 503114-39-4 503114-40-7 503114-42-9 503114-43-0 503114-44-1 503114-45-2 503114-46-3 503114-47-4 503114-48-5 503114-49-6 503114-50-9 503114-51-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitor; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (Manduca sexta))

IT 5255-04-9 21213-74-1 23314-84-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(juvenile hormone; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (Manduca sexta))

IT 65095-03-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(substrate, kinetic parameters; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (Manduca sexta))

IT 69106-46-3P, Juvenile hormone **epoxide hydrolase**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (Manduca sexta))

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

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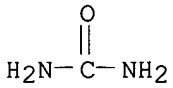
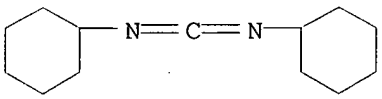
IT **57-13-6**, Urea, biological studies **538-75-0**
2387-23-7, 1,3-**Dicyclohexylurea**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; urea and amide-based inhibitors of juvenile hormone **epoxide hydrolase** of tobacco hornworm (Manduca sexta))

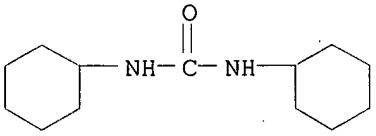
RN 57-13-6 HCAPLUS
CN Urea (8CI, 9CI) (CA INDEX NAME)



RN 538-75-0 HCAPLUS
CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)



RN 2387-23-7 HCAPLUS
CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



L90 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:340739** HCAPLUS
DN **138:49365**
TI Structural refinement of inhibitors of urea-based soluble **epoxide hydrolases**
AU Morisseau, Christophe; Goodrow, Marvin H.; Newman, John W.; Wheelock, Craig E.; Dowdy, Deanna L.; **Hammock, Bruce D.**
CS Department of Entomology, University of California, Davis, CA, 95616, USA
SO Biochemical Pharmacology (2002), 63(9), 1599-1608
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal
LA English
CC 1-3 (Pharmacology)
AB The sol. **epoxide hydrolase** (sEH) is involved in the metab. of arachidonic, linoleic, and other fatty acid epoxides, endogenous chem. mediators that play an important role in blood pressure regulation and inflammation. 1,3-Disubstituted ureas, carbamates, and amides are new potent and stable inhibitors of sEH. However, the poor soly. of the lead compds. limits their use. Inhibitor structure-activity relationships were investigated to better define the structural requirements for inhibition and to identify points in the mol. topog. that could accept polar groups without diminishing inhibition potency. Results indicate that

lipophilicity is an important factor controlling inhibitor potency. Polar groups could be incorporated into one of the alkyl groups without loss of activity if they were placed at a sufficient distance from the urea function. The resulting compds. had a 2-fold higher water soly. These findings will facilitate the rational design and optimization of sEH inhibitors with better phys. properties.

ST urea inhibitor prepn structure activity lipophilicity **epoxide hydrolase**

IT Blood pressure
Crystal structure
Drug design
Human
Lipophilicity
Mouse
Solubility
Structure-activity relationship
(structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)

IT **9048-63-9, Epoxide hydrolase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)

IT **2387-23-7** 287185-29-9
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)

IT 886-59-9P 1145-53-5P 1220-01-5P 2222-58-4P 13074-28-7P
17427-95-1P 29559-44-2P 38652-23-2P 62972-70-7P 72802-46-1P
75461-45-9P 89609-46-1P 108195-84-2P 120615-85-2P 124949-24-2P
148806-87-5P 179539-07-2P 195451-88-8P 200058-85-1P 200059-00-3P
201349-42-0P 401589-91-1P **402939-18-8P** 479412-88-9P
479412-91-4P 479413-00-8P 479413-14-4P 479413-19-9P 479413-36-0P
479413-39-3P 479413-45-1P 479413-50-8P 479413-53-1P 479413-55-3P
479413-57-5P 479413-59-7P 479413-61-1P 479413-63-3P 479413-65-5P
479413-68-8P **479413-70-2P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)

IT 124-22-1, Dodecylamine 3173-53-3, Cyclohexyl isocyanate 5452-37-9, Cyclooctylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD

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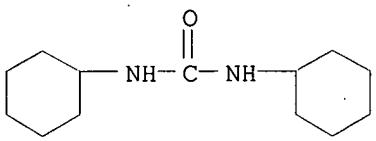
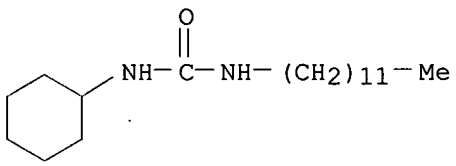
IT **9048-63-9, Epoxide hydrolase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **2387-23-7**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)
RN 2387-23-7 HCAPLUS
CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)

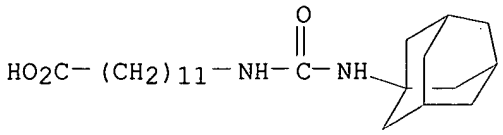


IT **402939-18-8P 479413-70-2P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structural refinement of inhibitors of urea-based sol. **epoxide hydrolases**)
RN 402939-18-8 HCAPLUS
CN Urea, N-cyclohexyl-N'-dodecyl- (9CI) (CA INDEX NAME)



RN 479413-70-2 HCAPLUS
CN Dodecanoic acid, 12-[[(tricyclo[3.3.1.13,7]dec-1-ylamino)carbonyl]amino]-

(9CI) (CA INDEX NAME)



L90 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:200865** HCAPLUS
DN **137:88154**
TI Inhibitors of soluble **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation
AU Davis, Benjamin B.; Thompson, David A.; Howard, Laura L.; Morisseau, Christophe; **Hammock, Bruce D.; Weiss, Robert H.**
CS Division of Nephrology, Department of Internal Medicine, Cell and Developmental Biology Graduate Group, University of California, Davis, CA, 95616, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(4), 2222-2227
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 1-8 (Pharmacology)
Section cross-reference(s): 14
AB Atherosclerosis, in its myriad incarnations the foremost killer disease in the industrialized world, is characterized by aberrant proliferation of vascular smooth muscle (VSM) cells in part as a result of the recruitment of inflammatory cells to the blood vessel wall. The **epoxyeicosatrienoic** acids are synthesized from arachidonic acid in a reaction catalyzed by the cytochrome P 450 system and are vasoactive substances. Metab. of these compds. by **epoxide hydrolases** results in the formation of compds. that affect the vasculature in a pleiotropic manner. As an outgrowth of our observations that urea inhibitors of the sol. **epoxide hydrolase** (sEH) reduce blood pressure in spontaneously hypertensive rats as well as the findings of other investigators that these compds. possess antiinflammatory actions, we have examd. the effect of sEH inhibitors on VSM cell proliferation. We now show that the sEH inhibitor 1-**cyclohexyl**-3-**dodecyl urea** (CDU) inhibits human VSM cell proliferation in a dose-dependent manner and is assocd. with a decrease in the level of cyclin D1. In addn., **cis-epoxyeicosatrienoic** acid mimics the growth-suppressive activity of CDU; there is no evidence of cellular toxicity or apoptosis in CDU-treated cells when incubated with 20 .mu.M CDU for up to 48 h. These results, in light of the antiinflammatory and antihypertensive properties of these compds. that have been demonstrated already, suggest that the urea class of sEH inhibitors may be useful for therapy for diseases such as hypertension and atherosclerosis characterized by exuberant VSM cell proliferation and vascular inflammation.
ST **epoxyeicosatrienoate** CDU antiatherosclerotic antihypertensive antiinflammatory signaling; antihypertensive **epoxide hydrolase** inhibitor apoptosis metab **epoxyeicosatrienoic** acid
IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D1; inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)
IT Antiarteriosclerotics

(antiatherosclerotics; inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)

IT Anti-inflammatory agents
Antihypertensives
Apoptosis
Atherosclerosis
Cardiovascular agents
Human
Signal transduction, biological
(inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)

IT Blood vessel
(smooth muscle; inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)

IT Hypertension
(spontaneous; inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)

IT 9035-51-2, Cytochrome P 450, biological studies **9048-63-9**, **Epoxide hydrolase** 142243-02-5, MAP kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)

IT 80558-45-8D, epoxides **402939-18-8**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD

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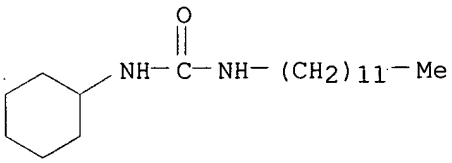
IT **9048-63-9, Epoxide hydrolase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **402939-18-8**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of sol. **epoxide hydrolase** attenuate vascular smooth muscle cell proliferation)
RN 402939-18-8 HCAPLUS
CN Urea, N-cyclohexyl-N'-dodecyl- (9CI) (CA INDEX NAME)



L90 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:161988** HCAPLUS
DN **136:338693**
TI Soluble **epoxide hydrolase** inhibition lowers arterial blood pressure in angiotensin II hypertension
AU Imig, John D.; Zhao, Xueying; Capdevila, Jorge H.; Morisseau, Christophe; **Hammock, Bruce D.**
CS Vascular Biology Center, Department of Physiology, Medical College of Georgia, Augusta, GA, USA
SO Hypertension (2002), 39(2, Pt. 2), 690-694
CODEN: HPRTDN; ISSN: 0194-911X
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 14-5 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1
AB **Epoxyeicosatrienoic** acids (EETs) have antihypertensive properties and play a part in the maintenance of renal microvascular function. A novel approach to increase EET levels is to inhibit **epoxide hydrolase** enzymes that are responsible for conversion of biol. active EETs to dihydroxyeicosatrienoic acids (DHETs) that are void of effects on the preglomerular vasculature. We hypothesized that inhibition of sol. **epoxide hydrolase** (sEH) would lower blood pressure in angiotensin II (Ang II) hypertension. Rat renal cortical tissue was harvested and urine collected 2 wk following implantation of an osmotic minipump contg. Ang II (60 ng/min). Renal cortical sEH protein expression was significantly higher in Ang II hypertension compared with normotensive animals. Likewise, urinary 14,15-DHET levels were significantly increased in hypertensive compared

with normotensive animals and averaged 8.1.+-.1.3 and 2.7.+-.1.1 ng/d; resp. In addnl. expts., the sEH inhibitor N-**cyclohexyl**-N-**dodecyl urea** (NCND; 3 mg/d) or vehicle (corn oil, 0.5 mL) was administered daily by i.p. injection starting on day 10. Administration of NCND for 4 days lowered systolic blood pressure by 30 mm Hg in Ang II hypertensive animals, whereas the corn oil vehicle had no effect on blood pressure in normotensive or Ang II hypertensive animals. Measurement of blood pressure by indwelling arterial catheters in conscious animals with free movement in their cages confirmed that NCND had antihypertensive properties. Arterial blood pressure averaged 119.+-.5 mm Hg in normotensive, 170.+-.3 mm Hg in hypertensive and 149.+-.10 mm Hg in NCND-treated, Ang II-infused animals. Administration of the potential metabolite of NCND, N-cyclohexylformamide to Ang II hypertensive rats did not lower the systolic blood pressure. These studies demonstrate that increased sEH expression in the Ang II hypertensive kidney leads to increased EET hydration. Moreover, sEH plays a role in the regulation of blood pressure, and inhibition of sEH during Ang II hypertension is antihypertensive.

ST **epoxide hydrolase** blood pressure angiotensin II hypertension; **epoxyeicosatrienoate** hydration dihydroxyeicosatrienoate urine **epoxide hydrolase** antihypertensive

IT Hydration, physiological
(increased renal sol. **epoxide hydrolase** leads to increased **epoxyeicosatrienoic** acid hydration in angiotensin II hypertension)

IT Kidney
Urine
(kidney sol. **epoxide hydrolase** levels are elevated in angiotensin II hypertension and assocd. with increased levels of urinary 14,15-dihydroxyeicosatrienoic acid)

IT Antihypertensives
Blood pressure
Hypertension
(sol. **epoxide hydrolase** inhibition in lowering arterial blood pressure in angiotensin II hypertension)

IT **97717-69-6, Epoxyeicosatrienoic** acid
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increased renal sol. **epoxide hydrolase** leads to increased **epoxyeicosatrienoic** acid hydration in angiotensin II hypertension)

IT 79551-81-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(kidney sol. **epoxide hydrolase** levels are elevated in angiotensin II hypertension and assocd. with increased levels of urinary 14,15-dihydroxyeicosatrienoic acid)

IT 11128-99-7, Angiotensin-II
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(sol. **epoxide hydrolase** inhibition in lowering arterial blood pressure in angiotensin II hypertension)

IT **9048-63-9, Epoxide hydrolase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sol.; sol. **epoxide hydrolase** inhibition in lowering arterial blood pressure in angiotensin II hypertension)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **97717-69-6**, **Epoxyeicosatrienoic** acid
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increased renal sol. **epoxide hydrolase** leads to increased **epoxyeicosatrienoic** acid hydration in angiotensin II hypertension)
RN 97717-69-6 HCAPLUS
CN Eicosatrienoic acid, epoxy- (9CI) (CA INDEX NAME)

CM 1

CRN 97717-68-5
CMF C20 H38 O3
CCI IDS

$HO_2C-(CH_2)_{18}-Me$

D1—O—D1

IT **9048-63-9**, **Epoxide hydrolase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sol.; sol. **epoxide hydrolase** inhibition in lowering arterial blood pressure in angiotensin II hypertension)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L90 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:863088** HCAPLUS
DN **136:116492**
TI Leukotoxin-Diol. A putative toxic mediator involved in acute respiratory distress syndrome

AU Zheng, Jiang; Plopper, Charles G.; Lakritz, Jeffery; Storms, David H.; **Hammock, Bruce D.**

CS Department of Pharmaceutical Sciences, School of Pharmacy, Bouve College of Health Sciences, Northeastern University, Boston, MA, 02115, USA

SO American Journal of Respiratory Cell and Molecular Biology (2001), 25(4), 434-438
CODEN: AJRBEL; ISSN: 1044-1549
PB American Thoracic Society
DT Journal
LA English
CC 14-4 (Mammalian Pathological Biochemistry)

AB Leukotoxin is clin. assocd. with acute respiratory distress syndrome (ARDS). Recently, we found that leukotoxin-diol, the hydrated product of leukotoxin, is more toxic than the parent leukotoxin in vitro. To test if this difference in the toxicity of leukotoxin and leukotoxin-diol exists in vivo, Swiss Webster mice were administered leukotoxin or leukotoxin-diol. All mice treated with leukotoxin-diol died of ARDS-like respiratory distress, whereas the animals exposed to leukotoxin at the same dose survived. Histopathol. evaluation of the lungs revealed massive alveolar edema and hemorrhage with interstitial edema around blood vessels in the lungs of mice treated with leukotoxin-diol, whereas the lungs of mice treated with identical doses of leukotoxin had perivascular edema only and little change in alveolar spaces. Immunohistochem. showed that the sol. **epoxide hydrolase** responsible for the hydrolysis of leukotoxin to its diol is concd. in the vascular smooth muscle of small and medium-sized pulmonary vessels. In addn., **4-phenylchalcone oxide**, an inhibitor of sol. **epoxide hydrolase**, was found to decrease the mortality induced by leukotoxin but had no effect on mortality induced by leukotoxin-diol. These studies provide strong in vivo evidence that leukotoxin may act as a protoxicant and that the corresponding diol is a putative toxic mediator involved in the development of ARDS.

ST leukotoxin diol toxic mediator respiration distress syndrome

IT Respiratory distress syndrome
(acute; leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

IT Lung
(alveolus; leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

IT Hydrolysis
(biol.; leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

IT Lung, disease
(injury; leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

IT Edema
Hemorrhage
(leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

IT Toxins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(leukotoxins; leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

IT Blood vessel
(smooth muscle; leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

IT 189191-41-1, Leukotoxin-Diol
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

IT **2403-28-3D, 4-Phenylchalcone, oxide**
9048-63-9, Epoxide hydrolase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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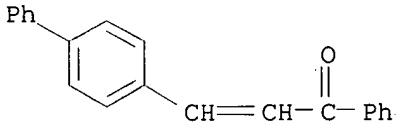
IT **2403-28-3D, 4-Phenylchalcone, oxide**
9048-63-9, Epoxide hydrolase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotoxin-diol. a putative toxic mediator involved in acute respiratory distress syndrome in mice)

RN 2403-28-3 HCAPLUS
CN 2-Propen-1-one, 3-[1,1'-biphenyl]-4-yl-1-phenyl- (9CI) (CA INDEX NAME)



RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L90 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:367801** HCAPLUS
DN **135:135057**
TI Pathways of **epoxyeicosatrienoic** acid metabolism in endothelial cells. Implications for the vascular effects of soluble **epoxide hydrolase** inhibition
AU Fang, Xiang; Kaduce, Terry L.; Weintraub, Neal L.; Harmon, Shawn; Teesch, Lynn M.; Morisseau, Christophe; Thompson, David A.; **Hammock, Bruce D.**; Spector, Arthur A.
CS Department of Biochemistry, College of Medicine, University of Iowa, Iowa City, IA, 52242, USA
SO Journal of Biological Chemistry (2001), 276(18), 14867-14874
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
AB **Epoxyeicosatrienoic** acids (EETs) are products of cytochrome P 450 epoxygenase that possess important vasodilating and anti-inflammatory properties. EETs are converted to the corresponding dihydroxyeicosatrienoic acid (DHET) by sol. **epoxide hydrolase** (sEH) in mammalian tissues, and inhibition of sEH has

been proposed as a novel approach for the treatment of hypertension. The authors obsd. that sEH is present in porcine coronary endothelial cells (PCEC), and the authors found that low concns. of N,N'-**dicyclohexylurea** (DCU), a selective sEH inhibitor, have profound effects on EET metab. in PCEC cultures. Treatment with 3 .mu.M DCU reduced cellular conversion of 14,15-EET to 14,15-DHET by 3-fold after 4 h of incubation, with a concomitant increase in the formation of the novel .beta.-oxidn. products 10,11-epoxy-16:2 and 8,9-epoxy-14:1. DCU also markedly enhanced the incorporation of 14,15-EET and its metabolites into PCEC lipids. The most abundant product in DCU-treated cells was 16,17-epoxy-22:3, the elongation product of 14,15-EET. Another novel metabolite, 14,15-epoxy-20:2, was present in DCU-treated cells. DCU also caused a 4-fold increase in release of 14,15-EET when the cells were stimulated with a calcium ionophore. Furthermore, DCU decreased the conversion of [3H]11,12-EET to 11,12-DHET, increased 11,12-EET retention in PCEC lipids, and produced an accumulation of the partial .beta.-oxidn. product 7,8-epoxy-16:2 in the medium. These findings suggest that in addn. to being metabolized by sEH, EETs are substrates for .beta.-oxidn. and chain elongation in endothelial cells and that there is considerable interaction among the three pathways. The modulation of EET metab. by DCU provides novel insight into the mechanisms by which pharmacol. or mol. inhibition of sEH effectively treats hypertension.

ST **epoxyeicosatrienoic** acid metab **epoxide** **hydrolase** oxidn coronary endothelium pig

IT Artery
(coronary, endothelium; pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide** **hydrolase** inhibition)

IT Blood vessel
(endothelium; pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

IT Antihypertensives
(pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

IT Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphoinositides
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

IT Oxidation
(.beta.-; pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

IT 26764-25-0, Octadecadienoic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(epoxy derivs.; pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

IT 506-32-1, Arachidonic acid 197508-62-6
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

IT **9048-63-9, Epoxide hydrolase**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

IT 7440-70-2, Calcium, biological studies 200960-01-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

IT 192461-94-2 192461-95-3 261967-98-0 261968-00-7 261968-01-8 351533-79-4 351533-80-7 351533-81-8
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

IT **2387-23-7, N,N'-Dicyclohexylurea**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
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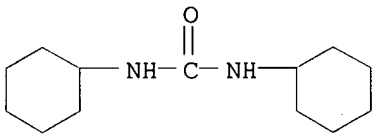
IT **9048-63-9**, **Epoxide hydrolase**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **2387-23-7**, N,N'-**Dicyclohexylurea**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(pathways of **epoxyeicosatrienoic** acid metab. in porcine coronary endothelial cells in relation to implications for vascular effects of sol. **epoxide hydrolase** inhibition)
RN 2387-23-7 HCAPLUS
CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



L90 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:878331** HCAPLUS
DN **134:54845**
TI Soluble **epoxide hydrolase** regulates hydrolysis of vasoactive **epoxyeicosatrienoic** acids
AU Yu, Zhigang; Xu, Fengyun; Huse, Linn M.; Morisseau, Christophe; Draper, Alison J.; Newman, John W.; Parker, Carol; Graham, LeRae; Engler, Marguerite M.; **Hammock, Bruce D.**; Zeldin, Darryl C.; Kroetz, Deanna L.
CS Department of Biopharmaceutical Sciences, School of Nursing, University of California, San Francisco, CA, USA
SO Circulation Research (2000), 87(11), 992-998
CODEN: CIRUAL; ISSN: 0009-7330
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 14-5 (Mammalian Pathological Biochemistry)
AB The cytochrome P 450-derived **epoxyeicosatrienoic** acids (EETs) have potent effects on renal vascular reactivity and tubular sodium and

water transport; however, the role of these eicosanoids in the pathogenesis of hypertension is controversial. The current study examd. the hydrolysis of the EETs to the corresponding dihydroxyeicosatrienoic acids (DHETs) as a mechanism for regulation of EET activity and blood pressure. EET hydrolysis was increased 5- to 54-fold in renal cortical S9 fractions from the spontaneously hypertensive rat (SHR) relative to the normotensive Wistar-Kyoto (WKY) rat. This increase was most significant for the 14,15-EET regioisomer, and there was a clear preference for hydrolysis of 14,15-EET over the 8,9- and 11,12-EETs. Increased EET hydrolysis was consistent with increased expression of sol. **epoxide hydrolase** (sEH) in the SHR renal microsomes and cytosol relative to the WKY samples. The urinary excretion of 14,15-DHET was 2.6-fold higher in the SHR than in the WKY rat, confirming increased EET hydrolysis in the SHR in vivo. Blood pressure was decreased 22 mm Hg 6 h after treatment of SHRs with the selective sEH inhibitor N,N'-**dicyclohexylurea**; this treatment had no effect on blood pressure in the WKY rat. These studies identify sEH as a novel therapeutic target for control of blood pressure. The identification of a potent and selective inhibitor of EET hydrolysis will be invaluable in sepg. the vascular effects of the EET and DHET eicosanoids.

ST **epoxide hydrolase** kidney **epoxyeicosatrienoate** hydrolysis blood pressure; hypertension eicosanoid metab **epoxide hydrolase** kidney

IT Kidney
(cortex; sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT Cytoplasm
(cytosol; sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT Antihypertensives
(sol. **epoxide hydrolase** inhibitors decrease of blood pressure in hypertension)

IT Blood pressure
(sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in blood pressure regulation)

IT Microsome
Urine
(sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT Eicosanoids
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT Hypertension
(spontaneous; sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT **2387-23-7**, N,N'-**Dicyclohexylurea**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sol. **epoxide hydrolase** inhibitor decrease of blood pressure in hypertension)

IT 81246-85-7 81276-02-0 81276-03-1
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC

(Process)
(sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT 79551-81-8 97717-67-4
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT **9048-63-9, Epoxide hydrolase**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

IT **97717-69-6, Epoxyeicosatrienoic** acid
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(triunsatd.; sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
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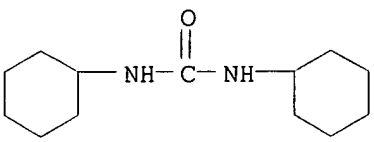
IT **2387-23-7, N,N'-Dicyclohexylurea**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sol. **epoxide hydrolase** inhibitor decrease of blood pressure in hypertension)

RN 2387-23-7 HCAPLUS

CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



IT **9048-63-9, Epoxide hydrolase**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **97717-69-6, Epoxyeicosatrienoic** acid
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(triunsatd.; sol. **epoxide hydrolase** of kidney regulation of hydrolysis of vasoactive **epoxyeicosatrienoic** acids in hypertension)
RN 97717-69-6 HCAPLUS
CN Eicosatrienoic acid, epoxy- (9CI) (CA INDEX NAME)

CM 1

CRN 97717-68-5
CMF C20 H38 O3
CCI IDS

$HO_2C-(CH_2)_{18}-Me$

D1—O—D1

L90 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:821596** HCAPLUS
DN **133:349972**
TI Preparation of ureas and related compounds as soluble **epoxide hydrolase** inhibitors.
IN **Hammock, Bruce D.**; Morisseau, Christophe H.; Zheng, Jiang; Goodrow, Marvin H.; Severson, Tonya; Sanborn, James
PA The Regents of the University of California, USA
SO U.S., 17 pp., Cont.-in-part of U. S. 5,955,496.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-17
NCL 514588000
CC 23-20 (Aliphatic Compounds)
Section cross-reference(s): 1, 5
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6150415	A	20001121	US 1999-252148	19990218
	US 5955496	A	19990921	US 1997-909523	19970812
	US 6174695	B1	20010116	US 1999-312207	19990514
	EP 1154764	A1	20011121	EP 2000-911767	20000210
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002540767	T2	20021203	JP 2000-599385	20000210
	US 6531506	B1	20030311	US 2000-721261	20001121
PRAI	US 1996-23397P	P	19960813		
	US 1997-909523	A2	19970812		
	US 1999-252148	A	19990218		
	WO 2000-US3495	W	20000210		

OS MARPAT 133:349972

AB R1R2XCOYR3R4 [I; X = C, O, N, S; Y = N, O, S; .gtoreq.1 of R1-R4 = H; R2 = H when X = N, R2 = null when X = S, O; R4 = H when Y = N, R4 = null when Y = S, O; R1, R3 = (substituted) alkyl, haloalkyl, cycloalkyl, aryl, acyl, heterocyclyl; and metabolites and degrdn. products thereof], were prepd. Thus, pentylamine in hexane was treated with octyl isocyanate followed by stirring and standing overnight to give 97% 1-octyl-3-pentylurea. The latter inhibited human sol. **epoxide hydrolase** with IC50 = 0.72 .mu.M. I may be used to purify, isolate, or inhibit **epoxide hydrolase**, and may be used in conjunction with herbicides, insecticides, and fungicides.

ST urea prepn soluble **epoxide hydrolase** inhibitor; thiocarbamate prepn soluble **epoxide hydrolase** inhibitor; antiinflammatory urea prepn; adult respiratory distress syndrome treatment urea

IT Respiratory distress syndrome
(adult, treatment; prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

IT Fungicides
(fungicides with **epoxide hydrolase** inhibitors; prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

IT Herbicides
(herbicides with **epoxide hydrolase** inhibitors; prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

IT Insecticides
(insecticides with **epoxide hydrolase** inhibitors; prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

IT Hormones, plant
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(plant growth regulators with **epoxide hydrolase** inhibitors; prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

IT Anti-inflammatory agents
Antitumor agents
(prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

IT **9048-63-9, Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibition, isolation, or purifn. of sol. **epoxide hydrolase**; prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)

IT 1220-01-5P 246165-77-5P 306770-63-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)
IT **538-75-0** 621-08-9 1212-29-9 2016-57-1, 1-Decanamine 2158-10-3 2222-58-4 **2387-23-7** 3567-62-2 20258-07-5 31510-11-9 78829-17-1 86446-52-8 91990-71-5 148806-83-1 196791-88-5 246165-79-7 306770-64-9 306770-65-0 306770-66-1 306770-67-2 306770-68-3 306770-69-4 306770-70-7 306770-71-8 306770-72-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)
IT 110-58-7, Pentylamine 1569-69-3, Cyclohexanethiol 3158-26-7, Octyl isocyanate 3173-53-3, Cyclohexyl isocyanate 5452-37-9, Cyclooctylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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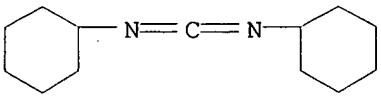
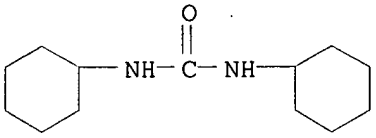
IT **9048-63-9, Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibition, isolation, or purifn. of sol. **epoxide hydrolase**; prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **538-75-0 2387-23-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of ureas and related compds. as sol. **epoxide hydrolase** inhibitors)
RN 538-75-0 HCAPLUS
CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)



RN 2387-23-7 HCAPLUS
CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



L90 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:503921** HCAPLUS
DN **131:280999**
TI Potent urea and carbamate inhibitors of soluble **epoxide hydrolases**
AU Morisseau, Christophe; Goodrow, Marvin H.; Dowdy, Deanna; Zheng, Jiang; Greene, Jessica F.; Sanborn, James R.; **Hammock, Bruce D.**
CS Department of Entomology, University of California, Davis, CA, 95616, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(16), 8849-8854
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 1-3 (Pharmacology)
Section cross-reference(s): 7, 25
AB The sol. **epoxide hydrolase** (sEH) plays a significant role in the biosynthesis of inflammation mediators as well as xenobiotic transformations. Herein, the authors report the discovery of substituted ureas and carbamates as potent inhibitors of sEH. Some of these selective, competitive tight-binding inhibitors with nanomolar Ki values interacted stoichiometrically with the homogeneous recombinant murine and human sEHs. These inhibitors enhance cytotoxicity of trans-stilbene oxide, which is active as the epoxide, but reduce cytotoxicity of leukotoxin, which is activated by **epoxide hydrolase** to its toxic diol. They also reduce toxicity of leukotoxin in vivo in mice and prevent symptoms suggestive of acute respiratory distress syndrome. These potent inhibitors may be valuable tools for testing hypotheses of involvement of diol and epoxide lipids in chem. mediation in vitro or in vivo systems.
ST **epoxide hydrolase** inhibitor urea carbamate structure
IT Respiratory distress syndrome
(adult, acute; potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)
IT Lipids, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(diol and epoxide; potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

IT Structure-activity relationship
(enzyme-inhibiting, **epoxide hydrolases**-inhibiting; potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

IT Toxins
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(leukotoxins, cytotoxicity; potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

IT Enzyme kinetics
(of inhibition; potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

IT 1439-07-2, trans-Stilbene oxide
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cytotoxicity; potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

IT 246165-79-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

IT **57-13-6**, Urea, biological studies 64-10-8, N-Phenylurea 102-04-5 102-06-7, N,N'-Diphenylguanidine 102-09-0 **538-75-0**, **Dicyclohexylcarbodiimide** 603-54-3 611-92-7 612-01-1 623-95-0, N,N'-Dipropylurea 722-01-0 1212-29-9, N,N'-Dicyclohexylthiourea **2387-23-7**, N,N'-**Dicyclohexylurea** 4559-87-9 13074-28-7 20258-07-5 31510-11-9 36102-06-4 82389-34-2 246165-77-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

IT **9048-63-9, Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

IT 2038-57-5, Benzenepropanamine 3173-53-3, Cyclohexylisocyanate
RL: RCT (Reactant); RACT (Reactant or reagent)
(potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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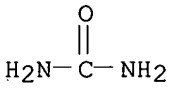
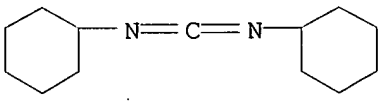
IT **57-13-6**, Urea, biological studies **538-75-0**, **Dicyclohexylcarbodiimide 2387-23-7**, N,N'-**Dicyclohexylurea**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)

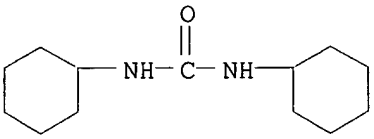
RN 57-13-6 HCAPLUS
CN Urea (8CI, 9CI) (CA INDEX NAME)



RN 538-75-0 HCAPLUS
CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)



RN 2387-23-7 HCAPLUS
CN Urea, N,N'-dicyclohexyl- (9CI) (CA INDEX NAME)



IT **9048-63-9, Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(potent urea and carbamate inhibitors of sol. **epoxide hydrolases** in relation to structure and role of diol and epoxide lipids and treatment of acute respiratory distress syndrome)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L90 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **1998:554776** HCAPLUS
DN **129:256849**
TI Mechanism of mammalian soluble **epoxide hydrolase** inhibition by **chalcone oxide** derivatives
AU Morisseau, Christophe; Du, Gehua; Newman, John W.; **Hammock, Bruce D.**
CS Department of Entomology and Department of Environmental Toxicology, University of California, Davis, CA, 95616, USA
SO Archives of Biochemistry and Biophysics (1998), 356(2), 214-228
CODEN: ABBIA4; ISSN: 0003-9861
PB Academic Press
DT Journal
LA English
CC 7-3 (Enzymes)
AB A series of substituted **chalcone oxides** (1,3-diphenyl-2-oxiranyl propanones) and structural analogs was synthesized to investigate the mechanism by which they inhibit sol. **epoxide hydrolases** (sEH). The inhibitor potency and inhibition kinetics were evaluated using both murine and human recombinant sEH. Inhibition kinetics were well described by the kinetic models of A. R. Main (1982, in Introduction to Biochem. Toxicol., pp. 193-223, Elsevier, New York) supporting the formation of a covalent enzyme-inhibitor intermediate with a half-life inversely proportional to inhibitor potency. Structure-activity relationships describe active-site steric constraints and support a mechanism of inhibition consistent with the electronic stabilization of the covalent enzyme-inhibitor intermediate. The electronic effects induced by altering the ketone functionality and the para-substitution of the Ph attached to the epoxy C1 (i.e., the .alpha.-carbon) had the greatest influence on inhibitor potency. The direction of the obsd. influence was reversed for the inhibitory potency of glycidol (1-phenyl-2-oxiranylpropanol) derivs. Recent insights into the mechanism of **epoxide hydrolase** activity are combined with these exptl. results to support a proposed mechanism of sEH inhibition by **chalcone oxides**. (c) 1998 Academic Press.
ST **epoxide hydrolase** inhibition **chalcone oxide** prepn
IT Structure-activity relationship
(enzyme-inhibiting; mechanism of mammalian sol. **epoxide hydrolase** inhibition by **chalcone oxide** derivs.)
IT QSAR (structure-activity relationship)
(mechanism of mammalian sol. **epoxide hydrolase**

inhibition by **chalcone oxide** derivs.)
IT Enzyme kinetics
(of inhibition; mechanism of mammalian sol. **epoxide hydrolase** inhibition by **chalcone oxide** derivs.)
IT **5411-12-1** 5633-36-3 6969-02-4 29425-81-8 32046-97-2
32047-01-1 32753-95-0 38860-42-3 40327-51-3 40327-54-6
40327-57-9 40327-58-0 42846-54-8 51477-11-3 55456-93-4
73354-53-7 93900-17-5 112711-73-6 131138-95-9 137487-67-3
147316-82-3 155190-86-6 203925-63-7 203925-65-9 213698-84-1
213698-85-2 213698-86-3 213698-87-4 213698-88-5 213698-89-6
213698-90-9 213698-91-0 213698-92-1 213698-93-2 213698-94-3
213698-95-4 213698-96-5 213698-97-6 213698-99-8 213699-01-5
213699-02-6 213699-04-8 213699-05-9 213699-06-0 213699-07-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mechanism of mammalian sol. **epoxide hydrolase** inhibition by **chalcone oxide** derivs.)
IT **9048-63-9, Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mechanism of mammalian sol. **epoxide hydrolase** inhibition by **chalcone oxide** derivs.)
IT 203925-64-8P 213698-98-7P 213699-00-4P 213699-03-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of substituted **chalcone oxides** and structural analogs for investigating their mechanism of **epoxide hydrolase** inhibition)
IT 67-36-7 98-86-2, reactions **2403-28-3, 4-Phenylchalcone** 4663-33-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant in prepn. of substituted **chalcone oxides** and structural analogs for investigating their mechanism of **epoxide hydrolase** inhibition)
IT 13677-55-9P 213699-08-2P 213699-09-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reactant in prepn. of substituted **chalcone oxides** and structural analogs for investigating their mechanism of **epoxide hydrolase** inhibition)
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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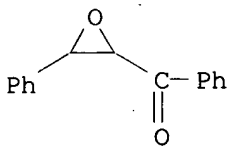
IT **5411-12-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mechanism of mammalian sol. **epoxide hydrolase** inhibition by **chalcone oxide** derivs.)

RN 5411-12-1 HCAPLUS
CN Methanone, phenyl(3-phenyloxiranyl)- (9CI) (CA INDEX NAME)



IT **9048-63-9, Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mechanism of mammalian sol. **epoxide hydrolase** inhibition by **chalcone oxide** derivs.)

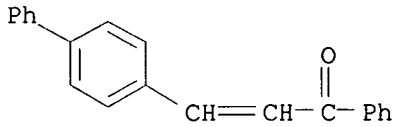
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **2403-28-3, 4-Phenylchalcone**
RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant in prepn. of substituted **chalcone oxides** and structural analogs for investigating their mechanism of **epoxide hydrolase** inhibition)

RN 2403-28-3 HCAPLUS
CN 2-Propen-1-one, 3-[1,1'-biphenyl]-4-yl-1-phenyl- (9CI) (CA INDEX NAME)



L90 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **1998:123974** HCAPLUS
DN **128:201056**
TI Methods of treating adult respiratory distress syndrome and other inflammatory diseases mediated by polyunsaturated lipid metabolites, and assays for **epoxide hydrolase** inhibitors
IN **Hammock, Bruce D.**; Moghaddam, Mehran F.; Cheek, Jeffrey M.; Borhan, Babak; Fergusson, James; Grant, David F.; Greene, Jessica F.; Matoba, Kazu; Zheng, Jiang; Sisemore, Marlene F.
PA Regents of the University of California, USA
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A01N033-02
ICS A01N043-20; A01N043-24; A01N037-02; A61K031-13; A61K031-23; A61K031-335
CC 1-7 (Pharmacology)
Section cross-reference(s): 7
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9806261	A1	19980219	WO 1997-US14385	19970813
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5955496	A	19990921	US 1997-909523	19970812
	AU 9740692	A1	19980306	AU 1997-40692	19970813
	EP 926951	A1	19990707	EP 1997-938335	19970813
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6174695	B1	20010116	US 1999-312207	19990514
PRAI	US 1996-23397P	P	19960813		
	US 1997-909523	A	19970812		
	WO 1997-US14385	W	19970813		

AB Methods are provided for treating inflammatory diseases mediated by polyunsatd. lipid metabolites by inhibiting **epoxide hydrolase**. The methods may be used for treating e.g. adult respiratory distress syndrome. Also provided are methods for assaying or screening the **epoxide hydrolase** inhibitors for inhibitory specificity and for toxicity, as well as novel biol. active THF diols of arachidonic acid, including antibodies thereto.
ST inflammatory disease treatment **epoxide hydrolase**

inhibitor; polyunsatd lipid metabolite inflammatory disease; screening
epoxide hydrolase inhibitor inflammation; ARDS
epoxide hydrolase inhibitor

IT Respiratory distress syndrome
(adult; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Lipids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkoxides; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Lung
(alveolus, epithelium, cells; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Nucleic acids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Insect (Insecta)
(cell line; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Lipids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(dihydroxy-; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Imides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diimides, lipophilic; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Immunoassay
(enzyme-linked immunosorbent assay; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Animal tissue culture
Anti-inflammatory agents
Biological transport
Drug screening
Spodoptera frugiperda
Structure-activity relationship
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Biological transport
(influx, calcium; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Baculoviridae
(insect cell line transfected with; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other

inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Skin
(keratinocyte; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Toxins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(leukotoxins, metabolites; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT Antibodies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(to arachidonate THF diol metabolites; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT 6088-36-4, Methyl isoleukotoxin diol 73889-55-1, Isoleukotoxin diol 189191-41-1, Leukotoxin diol 189191-42-2, Methyl leukotoxin diol
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT 112-63-0, Methyl linoleate 10547-36-1, Methyl isoleukotoxin 21019-43-2, Methyl leukotoxin 126639-26-7, Isoleukotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT 112-63-0D, Methyl linoleate, diepoxides **538-75-0**, **Dicyclohexylcarbodiimide 1885-07-0D**, derivs. **5411-12-1 5411-12-1D, Chalcone oxide**, derivs. 5633-36-3 6969-02-4 29425-81-8 32046-97-2 32753-95-0 40327-51-3 40327-54-6 40327-57-9 40327-58-0 42846-54-8 51477-11-3 203925-63-7 203925-64-8 203925-65-9 203925-66-0 203925-67-1 203925-68-2 203925-69-3 203925-70-6 203925-71-7 203925-72-8 203925-73-9 203925-74-0 203925-75-1 203925-76-2 203925-77-3 203925-78-4 203925-79-5 203925-80-8 203925-81-9 203925-82-0 203925-83-1 203925-84-2 203925-85-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT **9048-63-9, Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT 506-32-1D, Arachidonic acid, THF diols
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

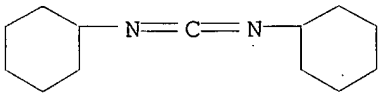
(Biological study); PROC (Process)
(intracellular; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

IT 506-32-1, Arachidonic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolites; **epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) D'Amato; US 5503990 A 1997 HCAPLUS

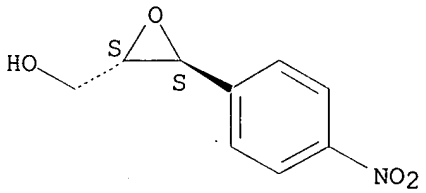
IT **538-75-0, Dicyclohexylcarbodiimide 1885-07-0D,** derivs. **5411-12-1 5411-12-1D, Chalcone oxide,** derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)

RN 538-75-0 HCAPLUS
CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)

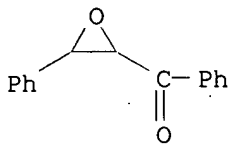


RN 1885-07-0 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

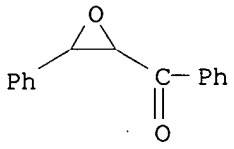
Absolute stereochemistry.



RN 5411-12-1 HCAPLUS
CN Methanone, phenyl(3-phenyloxiranyl)- (9CI) (CA INDEX NAME)



RN 5411-12-1 HCAPLUS
CN Methanone, phenyl(3-phenyloxiranyl)- (9CI) (CA INDEX NAME)



IT **9048-63-9, Epoxide hydrolase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**epoxide hydrolase** inhibitors, and screening thereof, for treatment of ARDS and other inflammatory diseases mediated by polyunsatd. lipid metabolites)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

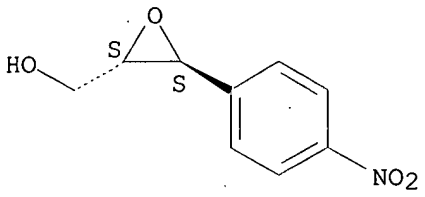
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L90 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **1993:443970** HCAPLUS
DN **119:43970**
TI The interaction of cytosolic **epoxide hydrolase** with chiral epoxides
AU Dietze, Eric C.; Kuwano, Eiichi; **Hammock, Bruce D.**
CS Dep. Entomol., Univ. California, Davis, CA, 95616, USA
SO International Journal of Biochemistry (1993), 25(1), 43-52
CODEN: IJBOBV; ISSN: 0020-711X
DT Journal
LA English
CC 7-3 (Enzymes)
AB The kinetic parameters of the cytosolic **epoxide hydrolase** were examd. with two sets of spectrophotometric substrates. The (2S, 3S)- and (2R, 3R)-enantiomers of 4-nitrophenyl trans-2,3-epoxy-3-phenylpropyl carbonate had a KM of 33 and 68 .mu.m and a Vmax of 16 and 27 .mu.mol/min/mg, resp. With the (2S,3S)- and (2R,3R)-enantiomers of 4-nitrophenyl trans-2,3-epoxy-3-(4-nitrophenyl)propyl carbonate, cytosolic **epoxide hydrolase** had a KM of 8.0 and 15 .mu.M and a Vmax of 7.8 and 5.0 .mu.mol/min/mg, resp. Glycidyl 4-nitrobenzoate had the lowest I50 of the compds. tested in the glycidyl 4-nitrobenzoate series (I50 = 140 .mu.M). The I50 of the (2R)-enantiomer was 3.7-fold higher. The inhibitor with the lowest I50 in the glycidol series, and the lowest I50 of any compd. tested, was (2S,3S)-3-(**4-nitrophenyl**)**glycidol** (I50 = 13.0 .mu.M). It also showed the greatest difference in I50 between the enantiomers (330-fold). All enantiomers of glycidyl 4-nitrobenzoates and trans-3-phenylglycidols gave differential inhibition of cytosolic **epoxide hydrolase**. However, neither the (S,S)-/(S)- or (R,R)-/(R)-enantiomer always had the lower I50. Addn. of one or more Me groups to either enantiomer of glycidyl 4-nitrobenzoate resulted in increased I50. However, addn. of a Me group to C2 of either enantiomer of 3-phenylglycidol resulted in a decreased I50. Finally, when the hydroxyl group of trans-3-(**4-nitrophenyl**)**glycidol** was esterified the I50 of the (2S,3S)- but not the (2R,3R)-enantiomer increased.
ST cytosol **epoxide hydrolase** stereochem; enantiomer glycidyl nitrobenzoate phenylglycidol **epoxide hydrolase**
IT Stereochemistry
(of **epoxide hydrolase** reaction with glycidyl nitrobenzoates and Ph glycidols and epoxy carbonates)
IT Michaelis constant
(of **epoxide hydrolase**, of cytosol)
IT Kinetics, enzymic

(of inhibition, of cytosolic **epoxide hydrolase** by glycidyl nitrobenzoate and Ph glycidol enantiomers)
IT Cytoplasm
(cytosol, **epoxide hydrolase** of, chiral epoxides reaction with and inhibition of)
IT Molecular structure-biological activity relationship
(**epoxide hydratase**-inhibiting, of glycidyl nitrobenzoate and Ph glycidol enantiomers)
IT Isomerism and Isomers
(optical, of glycidyl nitrobenzoates and Ph glycidols and epoxy carbonates, cytosolic **epoxide hydrolase** interaction with)
IT **9048-63-9, Epoxide hydrolase**
RL: PROC (Process)
(chiral epoxides reaction with and inhibition of, of cytosol)
IT 106268-95-5 106268-96-6 106268-97-7 106268-98-8 106948-05-4
107033-44-3 115362-13-5 115459-65-9 118200-96-7 130550-48-0
141700-91-6 141782-32-3
RL: BIOL (Biological study)
(cytosolic **epoxide hydrolase** inhibition by, structure in relation to)
IT 137461-28-0P 137461-29-1P 137493-99-3P 137494-00-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cytosolic **epoxide hydrolase** inhibition by, structure in relation to)
IT 147349-28-8P 147349-29-9P 147385-51-1P 147385-52-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cytosolic **epoxide hydrolase** reaction with)
IT 7693-46-1, 4-Nitrophenyl chloroformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Ph glycidol and **nitrophenyl glycidol** enantiomers)
IT 98-88-4, Benzoyl chloride 108-24-7, Acetic anhydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with **nitrophenyl glycidol** enantiomers)
IT **1885-07-0 37141-32-5**
RL: BIOL (Biological study)
(reaction with nitrophenyl chloroformate and acetic anhydride and benzoyl chloride and cytosolic **epoxide hydrolase** inhibition by)
IT 98819-68-2 104196-23-8, (2S,3S)-3-Phenylglycidol
RL: BIOL (Biological study)
(reaction with nitrophenyl chloroformate and cytosolic **epoxide hydrolase** inhibition by)
IT **9048-63-9, Epoxide hydrolase**
RL: PROC (Process)
(chiral epoxides reaction with and inhibition of, of cytosol)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

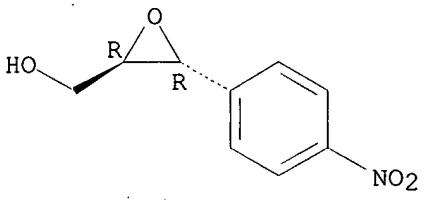
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **1885-07-0 37141-32-5**
RL: BIOL (Biological study)
(reaction with nitrophenyl chloroformate and acetic anhydride and benzoyl chloride and cytosolic **epoxide hydrolase** inhibition by)
RN 1885-07-0 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 37141-32-5 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L90 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **1993:208242** HCAPLUS
DN **118:208242**
TI Inhibition of **epoxide hydrolase** from human, monkey, bovine, rabbit and murine liver by trans-3-phenylglycidols
AU Dietze, Eric C.; Casas, Josefna; Kuwano, Eiichi; **Hammock, Bruce D.**
CS Dep. Entomol. Environ. Toxicol., Univ. California, Davis, CA, 95616, USA
SO Comparative Biochemistry and Physiology, Part B: Biochemistry & Molecular Biology (1993), 104B(2), 309-14
CODEN: CBPBB8; ISSN: 0305-0491
DT Journal
LA English
CC 7-3 (Enzymes)
Section cross-reference(s): 13
AB trans-3-Phenylglycidols were potent inhibitors of cytosolic **epoxide hydrolases** in all species tested. The order of inhibitor potency varied from species to species but trans-3-(**4-nitrophenyl)glycidols** were always the most potent inhibitors tested for cytosolic **epoxide hydrolase**. The S,S-enantiomer was a more potent cytosolic **epoxide hydrolase** inhibitor than the R,R-enantiomer when a free hydroxyl group was present. However, (2R,3R)-1-benzoyloxy-2,3-epoxy-3-(4-nitrophenyl)propane was always a better inhibitor than the (2S,3S)-enantiomer. All microsomal **epoxide hydrolases** were poorly inhibited by the trans-3-phenylglycidols, and related compds., tested. The best new microsomal **epoxide hydrolase** inhibitor tested was (1S,2S)-1-phenylpropylene oxide which gave 18-63% inhibition, at 2 mM, depending on the species tested.
ST mammal liver **epoxide hydrolase** inhibition phenylglycidol
IT Microsome
(**epoxide hydrolase** of, of mammalian liver, phenylglycidols inhibition of, species differences in and structure in relation to)
IT Liver, composition
(**epoxide hydrolases** of cytosol and microsome of, of mammals, phenylglycidols inhibition of, species differences in and structure in relation to)
IT Cattle

Macaca mulatta
Mouse
Rabbit
(**epoxide hydrolases** of liver cytosol and microsome of, phenylglycidols inhibition of, other mammals comparison with and structure in relation to)

IT Mammal
(**epoxide hydrolases** of liver cytosol and microsome of, phenylglycidols inhibition of, species differences in and structure in relation to)

IT Cytoplasm
(cytosol, **epoxide hydrolase** of, of mammalian liver, phenylglycidols inhibition of, species differences in and structure in relation to)

IT Molecular structure-biological activity relationship
(**epoxide hydratase**-inhibiting, of phenylglycidols)

IT **1885-07-0** 4518-66-5 14212-54-5 **37141-32-5**
98819-68-2 104196-23-8 137461-29-1 137494-00-9
RL: BIOL (Biological study)
(**epoxide hydrolases** of mammalian liver cytosol and microsome inhibition by, species differences in and structure in relation to)

IT 112711-73-6 137461-30-4 147316-82-3
RL: BIOL (Biological study)
(**epoxide hydrolases** of mammalian liver cytosol inhibition by, species differences in and structure in relation to)

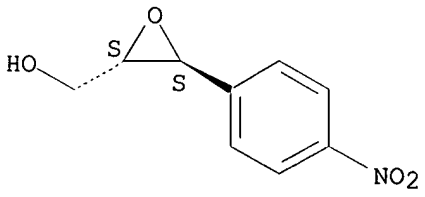
IT 286-20-4, Cyclohexene oxide
RL: BIOL (Biological study)
(**epoxide hydrolases** of mammalian liver microsome inhibition by, species differences in and structure in relation to)

IT **9048-63-9, Epoxide hydrolase**
RL: BIOL (Biological study)
(inhibition of cytosolic and microsomal, of mammalian liver by phenylglycidols, species differences in and structure in relation to)

IT **1885-07-0 37141-32-5**
RL: BIOL (Biological study)
(**epoxide hydrolases** of mammalian liver cytosol and microsome inhibition by, species differences in and structure in relation to)

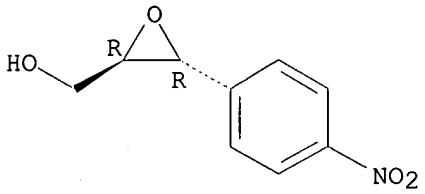
RN 1885-07-0 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 37141-32-5 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



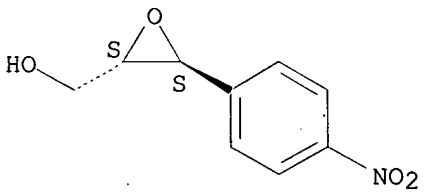
IT **9048-63-9, Epoxide hydrolase**
RL: BIOL (Biological study)
(inhibition of cytosolic and microsomal, of mammalian liver by phenylglycidols, species differences in and structure in relation to)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L90 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2003 ACS
AN **1991:672840** HCAPLUS
DN **115:272840**
TI Inhibition of cytosolic **epoxide hydrolase** by trans-3-phenylglycidols
AU Dietze, Eric C.; Kuwno, Eiichi; Casas, Josefina; **Hammock, Bruce D.**
CS Dep. Entomol., Univ. California, Davis, CA, 95616, USA
SO Biochemical Pharmacology (1991), 42(6), 1163-75
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
CC 4-3 (Toxicology)
Section cross-reference(s): 27
AB The inhibition of murine cytosolic **epoxide hydrolase** was studied with both racemic and enantiomerically pure trans-3-phenylglycidols. These compds. are the first enantioselective, slow binding inhibitors of cytosolic **epoxide hydrolase**. The (2S,3S)-3-phenylglycidol enantiomer was always a better inhibitor than the (2R,3R)-enantiomer. When the I50 values of (2S,3S)- and (2R,3R)-3-(**4-nitrophenyl**)**glycidol** were compared, the (2S,3S)-enantiomer was at least a 750-fold better inhibitor (I50 = 1.6 .mu.M) than the (2R,3R)-enantiomer (I50 = 1200 .mu.M), and it was the most potent inhibitor tested in the 3-phenylglycidol series. If the hydroxyl group of the glycidol was masked or converted to another functionality, the potency of the inhibitor decreased and the (2S,3S)-enantiomer was not necessarily the better inhibitor. In addn., trans-3-phenylglycidols demonstrated slow binding inhibition of cytosolic **epoxide hydrolase**. Inhibitors without a hydroxyl group, or with a blocked hydroxyl group, were not slow binding inhibitors. These results suggested that the hydroxyl group was important in both enantioselectivity and time dependence of inhibition of cytosolic **epoxide hydrolase** by trans-3-phenylglycidols. The hydration pattern of (2S,3S)- and (2R,3R)-2,3-epoxy-3-(**4-nitrophenyl**)**glycidol** by cytosolic **epoxide hydrolase** also differed. When incorporation of [18O] from water catalyzed by cytosolic **epoxide hydrolase** was measured, the (2S,3S)-enantiomer gave 12% incorporation into the benzylic carbon and the (2R,3R)-enantiomer gave 40% incorporation into the benzylic carbon. Finally, trans-3-phenylglycidols were poor inhibitors of microsomal **epoxide hydrolase**.
ST phenylglycidol **epoxide hydrolase** cytosol
IT Liver, composition
(**epoxide hydrolase** of cytosol and microsomes of, phenylglycidols effect on)

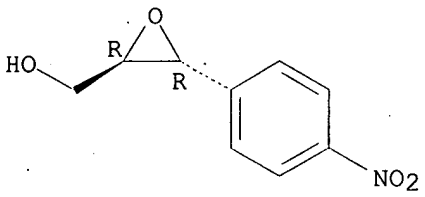
IT Microsome
(**epoxide hydrolase** of liver, phenylglycidols effect on)
IT Cytoplasm
(cytosol, **epoxide hydrolase** of liver, phenylglycidols effect on)
IT Molecular structure-biological activity relationship
(**epoxide hydratase**-inhibiting, by phenylglycidols, in liver cytosol and microsomes)
IT **1885-07-0** 4518-66-5 14212-54-5 **37141-32-5**
98819-68-2 104196-23-8 106948-05-4 115362-13-5
RL: BIOL (Biological study)
(**epoxide hydrolase** of liver cytosol response to)
IT **9048-63-9, Epoxide hydrolase**
RL: BIOL (Biological study)
(of liver cytosol and microsomes, phenylglycidols effect on)
IT 137461-26-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and oxidn. of)
IT 38860-42-3P 112711-73-6P 137461-27-9P 137461-28-0P 137461-29-1P
137487-67-3P 137493-99-3P 137494-00-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of and **epoxide hydrolase** of liver cytosol response to)
IT 555-16-8, 4-Nitrobenzaldehyde, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydroxypropyltriphenylphosphonium bromide)
IT 51860-45-8, 3-Hydroxypropyltriphenylphosphonium bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with nitrobenzaldehyde)
IT **5411-12-1, Chalcone oxide** 137461-30-4
137494-01-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(redn. of)
IT **1885-07-0 37141-32-5**
RL: BIOL (Biological study)
(**epoxide hydrolase** of liver cytosol response to)
RN 1885-07-0 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



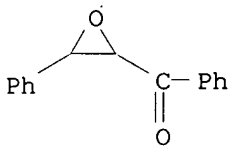
RN 37141-32-5 HCAPLUS
CN Oxiranemethanol, 3-(4-nitrophenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9048-63-9, Epoxide hydrolase**
RL: BIOL (Biological study)
(of liver cytosol and microsomes, phenylglycidols effect on)
RN 9048-63-9 HCAPLUS
CN Hydratase, epoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **5411-12-1, Chalcone oxide**
RL: RCT (Reactant); RACT (Reactant or reagent)
(redn. of)
RN 5411-12-1 HCAPLUS
CN Methanone, phenyl(3-phenyloxiranyl)- (9CI) (CA INDEX NAME)



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L98 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:290322** HCAPLUS
TI Inhibitors of soluble **epoxide hydrolase** attenuate **vascular smooth muscle cell** proliferation
AU Davis, Benjamin B.; Thompson, David A.; Howard, Laura L.; Morisseau, Christophe; **Hammock, Bruce D.; Weiss, Robert H.**
CS Division of Nephrology, Department of Internal Medicine, Cell and Developmental Biology Graduate Group, University of California, Davis, CA, 95616, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(7), 4752
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal; Errata
LA English
AB Unavailable

L98 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:12816** HCAPLUS
DN **130:163515**
TI 14,15-**Epoxyeicosatrienoic** acid inhibits prostaglandin E2 production in **vascular smooth muscle cells**
AU Fang, Xiang; Moore, Steven A.; Stoll, Lynn L.; Rich, Gretchen; Kaduce, Terry L.; Weintraub, Neal L.; Spector, Arthur A.
CS Departments of Biochemistry, University of Iowa, Iowa City, IA, 52242, USA
SO American Journal of Physiology (1998), 275(6, Pt. 2), H2113-H2121

CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
CC 2-9 (Mammalian Hormones)
AB 4,15-**Epoxyeicosatrienoic** acid (EET), a cytochrome P 450 epoxygenase product of arachidonic acid (AA), reduced PGE2 formation by 40-75% in porcine aortic and murine brain microvascular smooth muscle cells. The inhibition was reversed 6-10 h after removal of 14,15-EET from the medium and was regioisomeric specific; 8,9-EET produced a smaller effect, whereas 11,12- and 5,6-EET were ineffective. Although the cells converted 14,15-EET to 14,15-dihydroxyeicosatrienoic acid (14,15-DHET), 14,15-DHET did not inhibit PGE2 formation, and the 14,15-EET-induced inhibition was potentiated by **4-phenylchalcone oxide**, an **epoxide hydrolase** inhibitor. The inhibition occurred when substrate amts. of arachidonic acid (AA) were used and was not accompanied by enhanced prodn. of other prostaglandins, suggesting an effect on PGH synthase; however, in murine cells, 14,15-EET did not reduce PGH synthase mRNA or protein. Moreover, the 14,15-EET-induced decrease in PGE2 prodn. was overcome by increasing the concn. of AA, but not oleic acid (which is not a substrate for PGH synthase). These findings suggest that 14,15-EET competitively inhibits PGH synthase activity in **vascular smooth muscle cells**. The 14,15-EET-induced inhibition of PGE2 prodn. resulted in potentiation of platelet-derived growth factor-induced smooth muscle cell proliferation, suggesting that the competitive inhibition of PGH synthase by 14,15-EET can affect growth responses in smooth muscle cells.
ST **epoxyeicosatrienoate** PGE2 **vascular smooth muscle**
IT Artery
(aorta; **epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in **vascular smooth muscle cells**)
IT **Cell** proliferation
(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. and potentiation of PDGF-induced proliferation in **vascular smooth muscle cells** and mechanism therefor)
IT Platelet-derived growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. and potentiation of PDGF-induced proliferation in **vascular smooth muscle cells** and mechanism therefor)
IT Brain
(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in brain microvascular smooth muscle cells)
IT Blood vessel
(microvessel; **epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in brain microvascular smooth muscle cells)
IT Blood vessel
(**smooth muscle; epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in **vascular smooth muscle cells**)
IT 506-32-1, Arachidonic acid 81246-85-7 81276-03-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in **vascular smooth muscle cells**)
IT 79551-81-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in

vascular smooth muscle cells)
IT 363-24-6, Prostaglandin E2
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in **vascular smooth muscle cells**)
IT 39391-18-9, PGH synthase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**epoxyeicosatrienoic** acid inhibition of PGE2 prodn. in **vascular smooth muscle cells** and mechanism therefor)
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
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               E HAMMOCK B/AU
L7         542 S E3-E7
L8         153 S L4 AND L5-L7
L9          13 S CIS()(EPOXYEICOSATRIEN? OR EPOXY EICOSATRIEN?)
L10        478 S EPOXYEICOSATRIEN? OR EPOXY EICOSATRIEN?
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L18       8782 S DICYCLOHEXYLCARBODIIMIDE OR DICYLOHEXYL()(CARBODIIMIDE OR CAR
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L20         23 S L19 AND L8
L21          0 S L19 AND L12
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L24          0 S ADAMANT?(S)DODECYL?(S)UREA
L25         13 S CYCLOHEXYL(S)DODECYL(S)UREA
L26          0 S ADAMANT?(S)DODECYLUREA
L27          0 S CYCLOHEXYL(S)DODECYLUREA
L28        592 S DICYCLOHEXYLUREA OR DICYCLO HEXYL UREA OR DICYCLOHEXYL UREA O

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L44          1 S 538-75-0
L45          2 S 1885-07-0 OR 37141-32-5
L46         19 S C9H9NO4/MF AND OC2/ES AND 46.150.18/RID AND 2/NR
L47         14 S L46 AND NITROPHENYL
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L48           6 S L47 AND OXIRANEMETHANOL
L49           6 S L45,L48
L50             STR
L51       67542 S 638/RID
L52          50 S L50 SAM SUB=L51
L53        3291 S L50 FUL SUB=L51
L54             STR
L55           1 S L54 SAM SUB=L53
L56             STR L54
L57           1 S L56 SAM SUB=L53
L58          18 S L56 FUL SUB=L53
L59          13 S L58 AND 3/NR
L60           6 S L59 NOT ESTER
L61           5 S L60 AND 638.8/RID
                SAV L61 KWON056/A

     FILE 'HCAPLUS' ENTERED AT 17:21:45 ON 05 MAY 2003
L62           5 S L61

     FILE 'REGISTRY' ENTERED AT 17:22:17 ON 05 MAY 2003
L63           1 S 402939-18-8

     FILE 'HCAPLUS' ENTERED AT 17:22:45 ON 05 MAY 2003
L64           4 S L63
L65         339 S L29
L66        3258 S L44
L67          23 S L49
L68         155 S L34
L69          33 S L35
L70          68 S L36

     FILE 'REGISTRY' ENTERED AT 17:24:44 ON 05 MAY 2003
L71           1 S 97717-69-6
                E C20H32O3/MF
L72        2227 S E3
L73           7 S L72 AND EICOSATRIENOIC
L74           1 S L73 AND EPOXY
L75           6 S L73 NOT L74

     FILE 'HCAPLUS' ENTERED AT 17:26:09 ON 05 MAY 2003
L76          95 S L74
L77        3890 S L62,L64-L70,L76
L78          25 S L5-L7 AND L77
L79          22 S L78 AND L4
L80          17 S L79 AND L9-L28
L81           8 S L78,L79 NOT L80
                SEL DN AN 1 3
L82           2 S E1-E6
                SEL DN AN 1 3 4 7 8 11 12 13 15 16 L80
L83          10 S E7-E36
L84          12 S L82,L83 AND L77-L83
L85          13 S L80,L81 NOT L84
                SEL DN AN 1 3 9
L86           3 S L85 AND E37-E45
L87          15 S L84,L86

     FILE 'REGISTRY' ENTERED AT 17:36:10 ON 05 MAY 2003
L88           1 S 57-13-6

     FILE 'HCAPLUS' ENTERED AT 17:39:23 ON 05 MAY 2003
L89           2 S L88 AND L87
L90          15 S L87,L89
L91          33 S L4 AND L77
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L92          18 S L91 NOT L87
L93       11294 S VASCULAR (S) SMOOTH (S) (MUSCLE OR MUSCULAR) (S) CELL
L94       18771 S VASCULAR (S) SMOOTH (S) (MUSCLE OR MUSCULAR)
L95           6 S L93,L94 AND L4
L96           4 S L95 NOT L87
                SEL DN AN 3 4
L97           2 S L96 AND E46-E49
L98           2 S L97 AND L2-L28,L62,L64-L70,L76-L87,L89-L97
L99           1 S LIPID (S) ALKOXIDE AND L4
L100         32 S L4 AND L9,L10,L76
L101          7 S L4 AND L18,L66
L102         10 S L4 AND L13,L14,L67
L103         43 S L4 AND L15-L17,L68-L70
L104          7 S L100 AND L99,L101-L103
L105          5 S L104 NOT L87,L98
L106          8 S L103 AND L99-L102 NOT L87,L98
L107          8 S L105,L106
L108         55 S L99-L106 NOT L87,L98,L107
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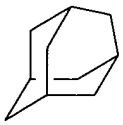
1 ANSWER 3642 OF 3648 REGISTRY COPYRIGHT 2003 ACS on STN
RN 281-23-2 REGISTRY
CN Tricyclo[3.3.1.13,7]decane (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Adamantane (6CI, 8CI)**
OTHER NAMES:
CN NSC 527913
FS 3D CONCORD
MF C10 H16
CI COM, RPS
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2512 REFERENCES IN FILE CA (1937 TO DATE)
286 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2512 REFERENCES IN FILE CAPLUS (1937 TO DATE)
45 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

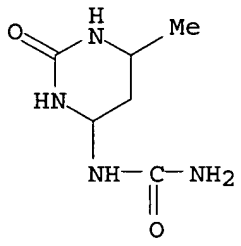
L15 ANSWER 6 OF 18 USPATFULL on STN
ACCESSION NUMBER: 87:45129 USPATFULL
TITLE: Anti-microbial compositions
INVENTOR(S): Fredrick, Jerome F., Bronx, NY, United States
PATENT ASSIGNEE(S): The Dodge Chemical Company, Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4675327		19870623
APPLICATION INFO.:	US 1983-483281		19830408 (6)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1977-786460, filed on 11 Apr 1977, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Robinson, Douglas W.
LEGAL REPRESENTATIVE: Conlin, David G., Williams, Gregory D.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 340
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Embalming preparations, which are far less noxious than previously known compositions, comprise a combination of a disinfectant and a plant growth regulating compound. The compositions achieve anti-microbial potency at concentrations of these ingredients far lower than the concentration levels of disinfectants found in known embalming preparations.

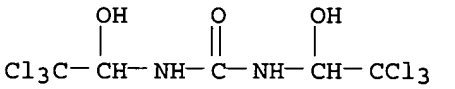
L8 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2003 ACS on STN
RN 1129-42-6 REGISTRY
CN Urea, (hexahydro-6-methyl-2-oxo-4-pyrimidinyl)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN (Hexahydro-6-methyl-2-oxo-4-pyrimidinyl)urea
CN 2-Oxo-4-methyl-6-ureidohexahydropyrimidine
CN **CDU**
CN Crotodure
CN Crotonylidenediurea
CN Cyclo-Di-Urea
CN Floranid
CN Floranit
CN Hexahydro-4-methyl-6-ureido-2-pyrimidone
CN NSC 13403
CN NSC 138171
FS 3D CONCORD
DR 12672-60-5, 37307-51-0
MF C6 H12 N4 O2
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CAOLD, CAPLUS, CHEMCATS, CHEMLIST, IFICDB, IFIPAT, IFIUDB, NIOSHTIC, PROMT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

127 REFERENCES IN FILE CA (1937 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
127 REFERENCES IN FILE CAPLUS (1937 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L9 ANSWER 25 OF 25 REGISTRY COPYRIGHT 2003 ACS on STN
RN 116-52-9 REGISTRY
CN Urea, N,N'-bis(2,2,2-trichloro-1-hydroxyethyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Urea, 1,3-bis(2,2,2-trichloro-1-hydroxyethyl)- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 1,3-Bis(1-hydroxy-2,2,2-trichloroethyl)urea
CN 1,3-Bis(2,2,2-trichloro-1-hydroxyethyl)urea
CN Crag Experimental Herbicide 2
CN Crag Herbicide 2
CN **DCU**
CN Dichloral urea
CN Dicloralurea
CN DKhM
CN EH2
CN Experimental Herbicide 2
CN NSC 32207
CN RC 9485
FS 3D CONCORD
DR 12765-19-4
MF C5 H6 Cl6 N2 O3
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, CA, CABA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, DDFU, DRUGU, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MSDS-OHS, NIOSHTIC, RTECS*, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

232 REFERENCES IN FILE CA (1937 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
233 REFERENCES IN FILE CAPLUS (1937 TO DATE)
19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

L4 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:277838 CAPLUS
DOCUMENT NUMBER: 132:303489
TITLE: Method of treating immunological disorders mediated by t-lymphocytes
INVENTOR(S): Erickson, David; Grob, Peter M.; Hoffman, Ann F.; Warren, Thomas C.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023060	A2	20000427	WO 1999-US24371	19991019
WO 2000023060	A3	20000908		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-104875P P 19981020

AB The use of **sol. epoxide hydrolase inhibitors** in the treatment of T-lymphocyte mediated immunol. disorders is described either as monotherapies or as part of combination therapies for such disorers. **Sol. epoxide hydrolase inhibitors** are e.g. N-[4-[5-ethyl-3-pyridin-3-yl-pyrazol-1-yl]-phenyl]nicotinamide.

6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 1994:498875 CAPLUS
DOCUMENT NUMBER: 121:98875
TITLE: Can we develop improved derivatives of valproic acid?
AUTHOR(S): Bialer, Meir; Haj-Yehia, Abdullah; Badir, Khalil; Hadad, Salim
CORPORATE SOURCE: Fac. Med., Heb. Univ. Jerusalem, Jerusalem, 91120, Israel
SOURCE: Pharmacy World & Science (1994), 16(1), 2-6
CODEN: PWSCED; ISSN: 0928-1231
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Valproic acid is one of the major antiepileptic drugs. A review with 35 refs. In animal models, valproate showed less anticonvulsant potency than the other three established antiepileptic drugs: phenobarbital, phenytoin and carbamazepine. In addn., two major side-effects, teratogenicity and hepatotoxicity, have been assocd. with valproate therapy. Due to the above and the shortage of new antiepileptic drugs there is a substantial need to develop improved derivs. of valproate. This paper analyzes three kinds of valproate derivs.: **valpromide**, the primary amide of valproate, and its analogs; monoester prodrugs of valproate and an active metabolite of valproate, 2-n-propyl-2-pentenoate. The comparative evaluation was carried out by pharmacokinetic and pharmacodynamic analyses in animals. From the data accumulated so far, the authors can conclude that 2-n-propyl-2-pentenoate and/or a **valpromide** isomer, which does not undergo amide-acid biotransformation and preferably is not an **epoxide hydrolase inhibitor**, may prove to be improved derivs. of the parent compd. valproic acid.

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:526069 CAPLUS
DOCUMENT NUMBER: 113:126069
TITLE: Unsubstituted amides: new class of potent inhibitors of human microsomal epoxide hydrolase
AUTHOR(S): Kerr, Bradley M.; Levy, Rene H.
CORPORATE SOURCE: Sch. Pharm., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: Drug Metabolism and Disposition (1990), 18(4), 540-2
CODEN: DMDSAI; ISSN: 0090-9556
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Various lipophilic amides, including **valpromide** and progabide, were potent inhibitors of epoxide hydrolase in human liver microsomes. Possible drug interactions are discussed.